

=> b reg

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STRUCTURE FILE UPDATES: 18 JUL 2006 HIGHEST RN 894196-03-3
DICTIONARY FILE UPDATES: 18 JUL 2006 HIGHEST RN 894196-03-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when
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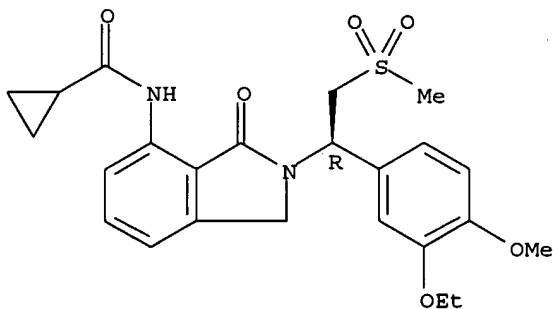
REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=> d ide can l9 tot

L9 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2006 ACS on STN
RN 340019-70-7 REGISTRY
ED Entered STN: 07 Jun 2001
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-2-(
(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA
INDEX NAME)
FS STEREOSEARCH
MF C24 H28 N2 O6 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 144:460857

REFERENCE 2: 143:472631

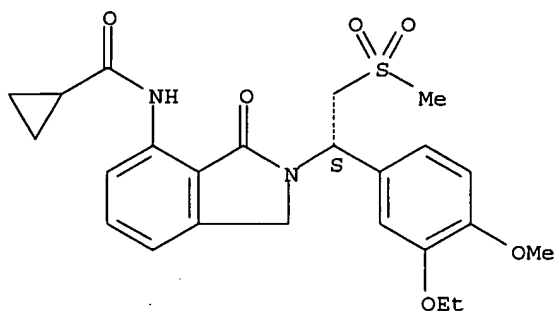
REFERENCE 3: 140:350585

REFERENCE 4: 140:42030

REFERENCE 5: 134:366799

L9 ANSWER 2 OF 3 REGISTRY ,COPYRIGHT 2006 ACS on STN
RN 340019-69-4 REGISTRY
ED Entered STN: 07 Jun 2001
CN Cyclopropanecarboxamide, N-[2-[(1S)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H28 N2 O6 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

6 REFERENCES IN FILE CA (1907 TO DATE)
6 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 145:55949

REFERENCE 2: 144:460857

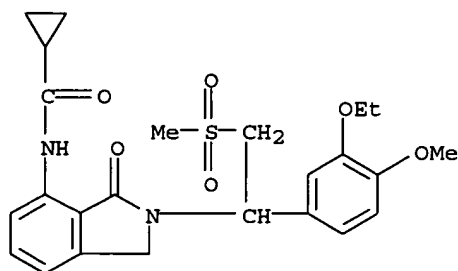
REFERENCE 3: 143:472631

REFERENCE 4: 140:350585

REFERENCE 5: 140:42030

REFERENCE 6: 134:366799

L9 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2006 ACS on STN
RN 340019-67-2 REGISTRY
ED Entered STN: 07 Jun 2001
CN Cyclopropanecarboxamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C24 H28 N2 O6 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

18 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 18 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 145:55949
 REFERENCE 2: 144:460857
 REFERENCE 3: 144:583
 REFERENCE 4: 144:582
 REFERENCE 5: 143:472631
 REFERENCE 6: 143:416245
 REFERENCE 7: 142:476229
 REFERENCE 8: 142:457121
 REFERENCE 9: 141:248733
 REFERENCE 10: 140:417943

=> b hcap

FILE 'HCAPLUS' ENTERED AT 08:44:29 ON 20 JUL 2006
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FILE COVERS 1907 - 20 Jul 2006 VOL 145 ISS 4
 FILE LAST UPDATED: 19 Jul 2006 (20060719/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all hitstr l17 tot

L17 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
 AN 2005:1259318 HCAPLUS
 DN 144:583
 ED Entered STN: 01 Dec 2005
 TI Methods and compositions using selective cytokine inhibitory drugs for treatment and management of cancers and other diseases
 IN Zeldis, Jerome B.
 PA Celgene Corporation, USA
 SO PCT Int. Appl., 89 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K-0031/40
 ICS A61K-0031/44
 CC 1-6 (Pharmacology)
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO2005112918	A1	20051201	2004WO-US14002	20040505
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRAI 2004WO-US14002 20040505

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2005112918	ICM	A61K-0031/40
	ICS	A61K-0031/44
	IPCI	A61K0031-40 [ICM,7]; A61K0031-44 [ICS,7]

OS MARPAT 144:583

AB Methods of treating, preventing and/or managing cancer as well as and diseases and disorders associated with, or characterized by, undesired angiogenesis are disclosed. Specific methods encompass the administration of a selective cytokine inhibitory drug alone or in combination with a second active ingredient. The invention further relates to methods of reducing or avoiding adverse side effects associated with chemotherapy, radiation therapy, hormonal therapy, biol. therapy or immunotherapy which comprise the administration of a selective cytokine inhibitory drug. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed.

ST antitumor cytokine inhibitor cancer therapy

IT Lymphoma

(B-cell diffuse, large cell; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Lymphoma

(B-cell, cutaneous; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Inflammation

(Crohn's disease; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Intestine, disease

(Crohn's; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Heat-shock proteins

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(HSP 90, inhibitors; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Sarcoma
(Kaposi's; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Mammary gland, neoplasm
(Paget's disease; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Bone, disease
(Paget's; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Skin, neoplasm
(T-cell lymphoma; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Antibodies and Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(VEGFR, HER-2; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Lymphoproliferative disorders
(Waldenstrom's macroglobulinemia; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Sarcoidosis
(Wegener's sarcoidosis; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Neuroglia, neoplasm
(anaplastic astrocytoma; cytokine inhibitors for treatment and management of cancers and other diseases)

IT neu (receptor)
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibody; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Drug resistance
(antitumor; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Infection
(bacterial, bacterial ulcer; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Ulcer
(bacterial, fungal, Mooren; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Therapy
(biol. therapy; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Carcinoma
(bladder transitional cell, metastatic; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Transplant and Transplantation
(bone marrow; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Oviduct
(cancer; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Artery, disease
(carotid, occlusion; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Eye, disease
(chronic vitritis, choroiditis, optic pits; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Intestine, neoplasm
(colorectal carcinoma; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Carcinoma
Intestine, neoplasm
(colorectal; cytokine inhibitors for treatment and management of

cancers and other diseases)

IT Eye
(cornea, transplant; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Transplant and Transplantation
(cornea; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Lymphoma
(cutaneous T-cell; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Acute myeloid leukemia

Amyloidosis

Angiogenesis

Angiogenesis inhibitors

Anti-inflammatory agents

Antiarthritics

Antibiotics

Antiglaucoma agents

Antirheumatic agents

Antitumor agents

Antiulcer agents

Behcet's syndrome

Bladder, neoplasm

Brain, neoplasm

Cardiovascular agents

Cord blood

Drug delivery systems

Endotoxemia

Fibrosis

Hematopoietic precursor cell

Hodgkin's disease

Human

Human herpesvirus

Human herpesvirus 3

Immunomodulators

Immunosuppressants

Immunotherapy

Lyme disease

Melanoma

Meningitis

Multiple myeloma

Neoplasm

Neuroglia, neoplasm

Osteoarthritis

Prophylaxis

Prostate gland, neoplasm

Radiotherapy

Retroviridae

Rheumatoid arthritis

Shock (circulatory collapse)

Sickle cell anemia

Sjogren syndrome

Surgery

Syphilis

Transplant and Transplantation

Transplant rejection
(cytokine inhibitors for treatment and management of cancers and other diseases)

IT Insulin-like growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cytokine inhibitors for treatment and management of cancers and other diseases)

IT Cytokines
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytokine inhibitors for treatment and management of cancers and other

diseases)

IT Corticosteroids, biological studies
Hemopoietins
Interferons
Interleukin 2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytokine inhibitors for treatment and management of cancers and other diseases)

IT Eye, disease
(diabetic retinopathy; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Reticuloendothelial system
(disease, histiocytosis, Langerhans cell; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Uterus, disease
(endometriosis; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Heart, disease
Kidney, disease
(failure; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Asbestos
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(fibrosis from; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Thyroid gland, neoplasm
(follicular cell carcinoma; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Fungi
(fungal ulcer; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Gingiva, disease
Inflammation
(gingivitis; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Neuroglia, neoplasm
(glioblastoma; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Sarcoma
(gynecol.; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Blood vessel, neoplasm
(hemangiopericytoma; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Carcinoma
(hepatocellular; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Liver, neoplasm
(hepatoma, metastatic; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Liver, neoplasm
(hepatoma; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Infection
(herpes simplex; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Infection
(herpes zoster; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Disease, animal
(histiocytosis, Langerhans cell; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Hormones, animal, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

- (hormonal therapy; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Neoplasm
 - (humoral hypercalcemia of malignancy; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Protozoa
 - (infection; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Epidermal growth factor receptors
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
 - (inhibitors; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Eye, disease
 - Inflammation
 - (keratitis; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Eye, disease
 - Inflammation
 - (keratoconjunctivitis, epidemic; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Myoma
 - (leiomyoma; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Myoma
 - Sarcoma
 - (leiomyosarcoma; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Lipids, biological studies
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
 - (lipid degeneration; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Anemia (disease)
 - (macrocytic anemia; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Thyroid gland, neoplasm
 - (medullary carcinoma; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Nervous system, neoplasm
 - (meningioma; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Mesothelium, neoplasm
 - (mesothelioma, malignant pleural effusion mesothelioma syndrome; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Brain, neoplasm
 - (metastasis; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Mammary gland, neoplasm
 - Melanoma
 - (metastatic; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Antibodies and Immunoglobulins
 - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (monoclonal, inhibitors; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Erythema
 - (multiforme; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Vision disorders
 - (myopia; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Astrocyte
 - (neoplasm, anaplastic astrocytoma; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Meninges

- (neoplasm, meningioma; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Oligodendrocyte
 - (neoplasm, oligodendroglioma, anaplastic; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Glaucoma (disease)
 - (neovascular; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Nerve, neoplasm
 - (neuroblastoma; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Endocrine system, neoplasm
 - (neuroendocrine system; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Lymphoma
 - (nodular; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Lymphoma
 - (non-Hodgkin's; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Lung, neoplasm
 - (non-small-cell carcinoma; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Artery, disease
- Vein, disease
 - (occlusion; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Histoplasma capsulatum
 - (ocular histoplasmosis; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Neuroglia, neoplasm
 - (oligodendroglioma, anaplastic; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Thyroid gland, neoplasm
 - (papillary carcinoma, serous; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Skin, disease
 - (pemphigoid; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Inflammation
- Periodontium, disease
 - (periodontitis; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Stem cell
 - (peripheral blood; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Eye, disease
 - (periretinal proliferation; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Peritoneum, neoplasm
 - (peritoneal carcinoma; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Disease, animal
 - (phlyectenulosis, fibrodysplasia ossificans, Terrien's marginal degeneration, Eale, best, stargart, pars planitis, hyperviscosity, rubeosis, 5q, mariginal keratolysis; cytokine inhibitors for treatment and management of cancers)
- IT Placenta
 - (placental blood; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Artery, disease
 - (polyarteritis; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Infection
 - (protozoan; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Skin, neoplasm
(pseudoxanthoma elasticum; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Carcinoma
(pulmonary non-small-cell; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Eye
(radial keratotomy; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Carcinoma
(rectal adenocarcinoma; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Intestine, neoplasm
(rectum, adenocarcinoma; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Drug toxicity
(reduction of; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Anemia (disease)
(refractory; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Antitumor agents
(resistance to; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Eye, disease
(retina, detachment, chronic; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Eye, disease
Inflammation
(retinitis; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Eye, disease
(retrolental fibroplasia; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Skin, disease
(rosacea; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Eye, disease
Inflammation
(scleritis; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Connective tissue, disease
(scleroderma; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Biliary tract, disease
Inflammation
(sclerosing cholangitis; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Animal tissue, disease
(soft, neoplasm, sarcoma; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Sarcoma
(soft-tissue; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Brain, disease
(stroke; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Lupus erythematosus
(systemic; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Carcinoma
(thyroid follicular cell; cytokine inhibitors for treatment and management of cancers and other diseases)

IT Carcinoma
(thyroid medullary; cytokine inhibitors for treatment and management of cancers and other diseases)

- IT Carcinoma
(thyroid papillary, serous; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Shock (circulatory collapse)
(toxic shock syndrome; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Infection
(toxoplasmosis; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Eye, disease
(trachoma; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Bladder, neoplasm
(transitional cell carcinoma, metastatic; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Bone marrow
(transplant; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Injury
(trauma; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Eye, disease
Inflammation
(uveitis, chronic; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Blood vessel, disease
Inflammation
(vasculitis, cutaneous; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Drugs
(veterinary; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Infection
(viral, HSV; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT Disease, animal
(wasting; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT 167886-76-2
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytokine inhibitors for treatment and management of cancers and other diseases)
- IT 50-02-2, Dexamethasone 57-22-7, Vincristine 147-94-4, Ara-C 148-82-3, Melphalan 362-07-2, 2-Methoxyestradiol 564-25-0, Doxycycline 4342-03-4, Dacarbazine 4759-48-2, Isotretinoin 6493-05-6, Pentoxifylline 11096-26-7, EPO 19545-26-7, Wortmannin 23214-92-8, Doxorubicin 71486-22-1, Vinorelbine 83869-56-1, Granulocyte-macrophage colony-stimulating factor 85721-33-1, Ciprofloxacin 97682-44-5, Irinotecan 114977-28-5, Taxotere 123948-87-8, Topotecan 143011-72-7, Granulocyte colony-stimulating factor 156586-89-9, Edrecolomab 174722-31-7, Rituximab 179324-69-7, Bortezomib 180288-69-1, Trastuzumab 183321-74-6, Erlotinib 184475-35-2, Gefitinib 185243-69-0, Etanercept 190977-41-4, Oblimersen 194413-58-6, Semaxanib 208921-02-2, Tositumomab 216974-75-3, Bevacizumab 265114-54-3, Telomestatin 340019-67-2 380610-27-5, Pertuzumab
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytokine inhibitors for treatment and management of cancers and other diseases)
- IT 9028-35-7
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, statins; cytokine inhibitors for treatment and management of cancers and other diseases)
- IT 9067-71-4, Lysophosphatidic acid acyltransferase 9076-57-7, Histone deacetylase 103843-29-4, Insulin-like growth factor-I receptor kinase

115926-52-8, PI3 kinase 137632-03-2, c-Met Tyrosine kinase
 159606-08-3, IκB Kinase 165245-96-5, p38 MAP kinase 329900-75-6,
 Cox-2 386705-49-3, Vascular endothelial growth factor receptor kinase
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitors; cytokine inhibitors for treatment and management of
 cancers and other diseases)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Duggan, M; US---6268378 B1 2001 HCAPLUS

(2) Zeldis; US2003438213 A1 2003

(3) Zeldis, J; WO2003097040 A1 2003 HCAPLUS

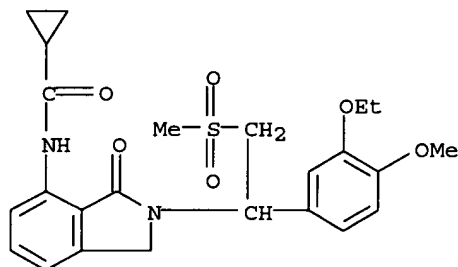
IT 340019-67-2

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)

(cytokine inhibitors for treatment and management of cancers and other
 diseases)

RN 340019-67-2 HCAPLUS

CN Cyclopropanecarboxamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)-2-
 (methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA
 INDEX NAME)



L17 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:428800 HCAPLUS

DN 140:417925

ED Entered STN: 27 May 2004

TI Methods and compositions using selective cytokine inhibitory drugs for
 treatment and management of cancers and other diseases

IN Zeldis, Jerome B.

PA Celgene Corporation, USA

SO PCT Int. Appl., 74 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K

CC 1-6 (Pharmacology)

Section cross-reference(s): 63

FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO2004043378	A2	20040527	WO 2003-US335545	20031106
	WO2004043378	A3	20040902		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

CA---2505131	AA	20040527	2003CA-2505131	20031106 <--
AU2003290652	A1	20040603	2003AU-0290652	20031106 <--
EP---1567154	A2	20050831	2003EP-0783234	20031106 <--
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BR2003016057	A	20050920	2003BR-0016057	20031106 <--
CN---1735412	A	20060215	CN 2003-80108390	20031106
JP2006508131	T2	20060309	2004JP-0551873	20031106 <--
US2006035955	A1	20060216	2005US-0534325	20050912 <--
AU2006202316	A1	20060622	2006AU-0202316	20060531
PRAI 2002US-424601P	P	20021106		
2003AU-0234626	A3	20030516		
2003WO-US35545	W	20031106	<--	

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004043378	ICM	A61K
	IPCI	A61K [ICM,7]
	IPCR	A61K0031-00 [I,A]; A61K0031-00 [I,C*]; A61K0031-40 [I,A]; A61K0031-40 [I,C*]; A61K0031-425 [I,A]; A61K0031-425 [I,C*]; A61K0031-445 [I,A]; A61K0031-445 [I,C*]; A61K0031-513 [I,C*]; A61K0031-515 [I,A]; A61K0045-00 [I,C*]; A61K0045-06 [I,A]
	ECLA	A61K031/00; A61K031/40; A61K031/425; A61K031/445; A61K031/515; A61K045/06; A61K031/40+M; A61K031/4035; A61K031/4035+M; A61K031/415; A61K031/415+M; A61K031/425+M; A61K031/44; A61K031/44+M; A61K031/454; A61K031/454+M
CA---2505131	IPCI	A61K0031-44 [ICM,7]; A61K0031-40 [ICS,7]; A61K0031-415 [ICS,7]; A61K0031-425 [ICS,7]
	IPCR	A61K0031-00 [I,A]; A61K0031-00 [I,C*]; A61K0031-40 [I,A]; A61K0031-40 [I,C*]; A61K0031-425 [I,A]; A61K0031-425 [I,C*]; A61K0031-445 [I,A]; A61K0031-445 [I,C*]; A61K0031-513 [I,C*]; A61K0031-515 [I,A]; A61K0045-00 [I,C*]; A61K0045-06 [I,A]
	ECLA	A61K031/40; A61K031/00; A61K031/40+M; A61K031/4035; A61K031/4035+M; A61K031/415; A61K031/415+M; A61K031/425; A61K031/425+M; A61K031/44; A61K031/44+M; A61K031/454; A61K031/454+M; A61K045/06
AU2003290652	IPCI	A61K0031-44 [ICM,7]; A61K0031-425 [ICS,7]; A61K0031-415 [ICS,7]; A61K0031-40 [ICS,7]
	IPCR	A61K0031-00 [I,A]; A61K0031-00 [I,C*]; A61K0031-40 [I,A]; A61K0031-40 [I,C*]; A61K0031-425 [I,A]; A61K0031-425 [I,C*]; A61K0031-445 [I,A]; A61K0031-445 [I,C*]; A61K0031-513 [I,C*]; A61K0031-515 [I,A]; A61K0045-00 [I,C*]; A61K0045-06 [I,A]
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BR2003016057	IPCI	A61K0031-44 [ICM,7]; A61K0031-425 [ICS,7]; A61K0031-415 [ICS,7]; A61K0031-40 [ICS,7]
	IPCR	A61K0031-00 [I,A]; A61K0031-00 [I,C*]; A61K0031-40 [I,A]; A61K0031-40 [I,C*]; A61K0031-425 [I,A]; A61K0031-425 [I,C*]; A61K0031-445 [I,A]; A61K0031-445 [I,C*]; A61K0031-513 [I,C*]; A61K0031-515 [I,A]; A61K0045-00 [I,C*]; A61K0045-06 [I,A]
	ECLA	A61K031/40; A61K031/00; A61K031/40+M; A61K031/4035; A61K031/4035+M; A61K031/415; A61K031/415+M;

A61K031/425; A61K031/425+M; A61K031/44; A61K031/44+M;
 A61K031/454; A61K031/454+M; A61K045/06
 CN--1735412 IPCI A61K0031-44 [I,A]; A61K0031-425 [I,A]; A61K0031-415
 [I,A]; A61K0031-40 [I,A]
 ECLA A61K031/40; A61K031/00; A61K031/40+M; A61K031/4035;
 A61K031/4035+M; A61K031/415; A61K031/415+M;
 A61K031/425; A61K031/425+M; A61K031/44; A61K031/44+M;
 A61K031/454; A61K031/454+M; A61K045/06
 JP2006508131 IPCI A61K0045-00 [I,A]; A61K0031-4035 [I,A]; A61K0031-403
 [I,C*]; A61P0035-00 [I,A]; A61P0043-00 [I,A]
 FTERM 4C084/AA17; 4C084/MA01; 4C084/NA14; 4C084/ZB052;
 4C084/ZB212; 4C084/ZB262; 4C086/AA01; 4C086/AA02;
 4C086/BC10; 4C086/MA01; 4C086/MA04; 4C086/NA14;
 4C086/ZB05; 4C086/ZB21; 4C086/ZB26
 US2006035955 IPCI A61K0031-4035 [I,A]; A61K0031-403 [I,C*]; A61K0038-19
 [I,A]; A61K0031-522 [I,A]; A61K0031-519 [I,C*]
 NCL 514/416.000
 AU2006202316 IPCI A61K0031-00 [I,C*]; A61K0031-40 [I,C*]; A61K0031-425
 [I,C*]; A61K0031-445 [I,C*]; A61K0031-4523 [I,C*];
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 [I,A]; A61K0031-00 [I,A]; A61K0031-40 [I,A];
 A61K0031-425 [I,A]; A61K0031-454 [I,A]; A61K0031-515
 [I,A]; A61K0045-06 [I,A]
 OS MARPAT 140:417925
 AB Methods for treating, preventing and/or managing cancer as well as and
 diseases and disorders associated with, or characterized by, undesired
 angiogenesis are disclosed. Specific methods encompass the administration
 of a selective cytokine inhibitory drug alone or in combination with a
 second active ingredient. The invention further discloses methods for
 reducing or avoiding adverse side effects associated with chemotherapy,
 radiation therapy, hormonal therapy, biol. therapy or immunotherapy which
 comprise the administration of a selective cytokine inhibitory drug.
 Pharmaceutical compns., single unit dosage forms, and kits suitable for
 use in methods of the invention are also disclosed.
 ST antitumor drug therapeutic cytokine inhibitor angiogenesis inhibition;
 adverse effect redn therapeutic cytokine inhibitor
 IT Disease, animal
 (5q- syndrome; cytokine inhibitors for treatment and management of
 cancers and other diseases, and use with other therapeutic means)
 IT Lymphoma
 (B-cell diffuse, large cell; cytokine inhibitors for treatment and
 management of cancers and other diseases, and use with other therapeutic
 means)
 IT Lymphoma
 (B-cell, cutaneous; cytokine inhibitors for treatment and management of
 cancers and other diseases, and use with other therapeutic means)
 IT Disease, animal
 (Best; cytokine inhibitors for treatment and management of cancers and
 other diseases, and use with other therapeutic means)
 IT Disease, animal
 (Eale; cytokine inhibitors for treatment and management of cancers and
 other diseases, and use with other therapeutic means)
 IT Sarcoma
 (Kaposi's; cytokine inhibitors for treatment and management of cancers
 and other diseases, and use with other therapeutic means)
 IT Ulcer
 (Mooren; cytokine inhibitors for treatment and management of cancers
 and other diseases, and use with other therapeutic means)
 IT Mammary gland, neoplasm
 (Paget's disease; cytokine inhibitors for treatment and management of
 cancers and other diseases, and use with other therapeutic means)
 IT Bone, disease
 (Paget's; cytokine inhibitors for treatment and management of cancers
 and other diseases, and use with other therapeutic means)
 IT Disease, animal
 (Scleritis; cytokine inhibitors for treatment and management of cancers

- and other diseases, and use with other therapeutic means)
- IT Disease, animal
(Stargart; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Skin, neoplasm
(T-cell lymphoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Disease, animal
(Terrien's marginal degeneration; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Lymphoproliferative disorders
(Waldenstrom's macroglobulinemia; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Disease, animal
(Wegener's sarcoidosis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Neuroglia, neoplasm
(anaplastic astrocytoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Drug resistance
(antitumor; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Infection
(bacterial, bacterial ulcer; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Therapy
(biol. therapy; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Carcinoma
(bladder transitional cell, metastatic; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Transplant and Transplantation
(bone marrow; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Oviduct
(cancer; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Artery, disease
(carotid, occlusion; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Eye, disease
(choroiditis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Eye, disease
(chronic vitritis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Intestine, neoplasm
(colorectal carcinoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Carcinoma
Intestine, neoplasm
(colorectal; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Eye
(cornea, transplant; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Transplant and Transplantation
(cornea; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Lymphoma

- (cutaneous T-cell; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Acute myeloid leukemia
- Amyloidosis
- Angiogenesis
- Angiogenesis inhibitors
- Anti-inflammatory agents
- Antiarthritics
- Antibiotics
- Antiglaucoma agents
- Antirheumatic agents
- Antitumor agents
- Antiulcer agents
- Behcet's syndrome
- Bladder, neoplasm
- Brain, neoplasm
- Cardiovascular agents
- Cord blood
- Drug delivery systems
- Endotoxemia
- Fibrosis
- Hematopoietic precursor cell
- Hodgkin's disease
- Human
- Human herpesvirus
- Human herpesvirus 3
- Immunomodulators
- Immunosuppressants
- Immunotherapy
- Lyme disease
- Melanoma
- Meningitis
- Multiple myeloma
- Neoplasm
- Neuroglia, neoplasm
- Osteoarthritis
- Prostate gland, neoplasm
- Radiotherapy
- Rheumatoid arthritis
- Shock (circulatory collapse)
- Sickle cell anemia
- Sjogren syndrome
- Surgery
- Syphilis
- Transplant and Transplantation
- Transplant rejection
- Ulcer
- (cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Cytokines
- RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
- (cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Corticosteroids, biological studies
- Hemopoietins
- Interferons
- Interleukin 2
- RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
- (cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Eye, disease
- (diabetic retinopathy; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Reticuloendothelial system

- (disease, histiocytosis, Langerhans cell; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Disease, animal
(fibrodysplasia ossificans; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Asbestos
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(fibrosis from; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Thyroid gland, neoplasm
(follicular cell carcinoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Fungi
(fungal ulcer; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Gingiva, disease
Inflammation
(gingivitis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Neuroglia, neoplasm
Neuroglia, neoplasm
(glioblastoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Sarcoma
(gynecol.; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Blood vessel, neoplasm
(hemangiopericytoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Carcinoma
(hepatocellular; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Liver, neoplasm
(hepatoma, metastatic; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Liver, neoplasm
(hepatoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Disease, animal
(histiocytosis, Langerhans cell; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Hormones, animal, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hormonal therapy; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Neoplasm
(humoral hypercalcemia of malignancy; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Disease, animal
(hyperviscosity syndromes; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Protozoa
(infection; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Eye, disease
Inflammation
(keratitis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Eye, disease

- Inflammation
(keratoconjunctivitis, epidemic; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Myoma
(leiomyoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Myoma
Sarcoma
(leiomyosarcoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(lipid degeneration; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Anemia (disease)
(macrocytic anemia; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Disease, animal
(mariginal keratolysis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Thyroid gland, neoplasm
(medullary carcinoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Nervous system, neoplasm
(meningioma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Mesothelium, neoplasm
(mesothelioma, malignant pleural effusion mesothelioma syndrome; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Brain, neoplasm
(metastasis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Mammary gland, neoplasm
Melanoma
(metastatic; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Erythema
(multiforme; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Vision disorders
(myopia; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Astrocyte
(neoplasm, anaplastic astrocytoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Meninges
(neoplasm, meningioma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Oligodendrocyte
(neoplasm, oligodendroglioma, anaplastic; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Glaucoma (disease)
(neovascular; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Nerve, neoplasm
(neuroblastoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Endocrine system, neoplasm
(neuroendocrine system; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)

- IT Lymphoma
(nodular; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Lymphoma
(non-Hodgkin's; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Lung, neoplasm
(non-small-cell carcinoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Artery, disease
- Vein, disease
(occlusion; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Histoplasma capsulatum
(ocular histoplasmosis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Neuroglia, neoplasm
(oligodendroglioma, anaplastic; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Eye, disease
(optic pits; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Thyroid gland, neoplasm
(papillary carcinoma, serous; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Disease, animal
(pars planitis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Skin, disease
(pemphigoid; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Inflammation
- Periodontium, disease
(periodontitis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Stem cell
(peripheral blood; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Eye, disease
(periretinal proliferation; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Peritoneum, neoplasm
(peritoneal carcinoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Disease, animal
(phlyctenulosis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Placenta
(placental blood; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Artery, disease
(polyarteritis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Skin, neoplasm
(pseudoxanthoma elasticum; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Carcinoma
(pulmonary non-small-cell; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)

- IT Eye
(radial keratotomy; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Carcinoma
(rectal adenocarcinoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Intestine, neoplasm
(rectum, adenocarcinoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Drug toxicity
(reduction of; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Anemia (disease)
(refractory; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Antitumor agents
(resistance to; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Eye, disease
(retina, detachment, chronic; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Eye, disease
Inflammation
(retinitis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Eye, disease
(retrolental fibroplasia; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Retroviridae
(retrovirus replication; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Skin, disease
(rosacea; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Disease, animal
(rubeosis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Disease, animal
(sarcoid; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Connective tissue, disease
(scleroderma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Biliary tract, disease
Inflammation
(sclerosing cholangitis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Animal tissue, disease
(soft, neoplasm, sarcoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Sarcoma
(soft-tissue; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Brain, disease
(stroke; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Lupus erythematosus
(systemic; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)

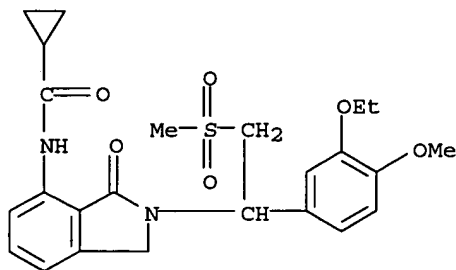
- IT Carcinoma
(thyroid follicular cell; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Carcinoma
(thyroid medullary; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Carcinoma
(thyroid papillary, serous; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Shock (circulatory collapse)
(toxic shock syndrome; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Infection
(toxoplasmosis; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Eye, disease
(trachoma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Bladder, neoplasm
(transitional cell carcinoma, metastatic; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Bone marrow
(transplant; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Injury
(trauma; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Eye, disease
Inflammation
(uveitis, chronic; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Blood vessel, disease
Inflammation
(vasculitis, cutaneous; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Drugs
(veterinary; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT Disease, animal
(wasting; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT 50-02-2, Dexamethasone 57-22-7, Vincristine 147-94-4, Ara-C 148-82-3, Melphalan 4342-03-4, Dacarbazine 4759-48-2, Isotretinoin 6493-05-6, Pentoxifylline 11096-26-7, Erythropoietin 23214-92-8, Doxorubicin 71486-22-1, Vinorelbine 83869-56-1, GM-CSF 85721-33-1, Ciprofloxacin 97682-44-5, Irinotecan 114977-28-5, Taxotere 123948-87-8, Topotecan 143011-72-7, G-CSF 167886-76-2 190977-41-4, Oblimersen 340019-67-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT 7631-86-9, Silica, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(fibrosis from; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT 329900-75-6, Cyclooxygenase 2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)
- IT 340019-67-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(cytokine inhibitors for treatment and management of cancers and other diseases, and use with other therapeutic means)

RN 340019-67-2 HCAPLUS

CN Cyclopropanecarboxamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)



L17 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:392056 HCAPLUS

DN 140:386062

ED Entered STN: 14 May 2004

TI Methods of using and compositions comprising selective cytokine inhibitory drugs for treatment and management of macular degeneration

IN Zeldis, Jerome B.

PA USA

SO U.S. Pat. Appl. Publ., 19 pp.

CODEN: USXXCO

DT Patent

LA English

IC ICM A61K-0038/21

ICS A61K-0039/395; A61K-0031/56; A61K-0031/545; A61K-0031/522;
A61K-0031/454; A61K-0031/557INCL 424085700; 424145100; 514171000; 514200000; 514012000; 514192000;
514263310; 514323000; 514573000

CC 1-12 (Pharmacology)

Section cross-reference(s): 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US2004091454	A1	20040513	2003US-0699110	20031030
	CA---2504263	AA	20040521	2003CA-2504263	20031031
	WO2004041181	A2	20040521	2003WO-US34535	20031031
	WO2004041181	A3	20050217		
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	AU2003285107	A1	20040607	2003AU-0285107	20031031
	EP---1567148	A2	20050831	2003EP-0779423	20031031
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	BR2003015889	A	20051004	2003BR-0015889	20031031
	CN---1731997	A	20060208	CN 2003-80108090	20031031
	JP2006509743	T2	20060323	2004JP-0550274	20031031

AU2004286824	A1	20050519	2004AU-0286824	20040428
CA---2543618	AA	20050519	2004CA-2543618	20040428
WO2005044269	A1	20050519	2004WO-US13253	20040428

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI 2002US-422900P	P	20021031
2003US-0699110	A	20031030
2003WO-US34535	W	20031031
2004WO-US13253	W	20040428

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2004091454	ICM	A61K-0038/21
	ICS	A61K-0039/395; A61K-0031/56; A61K-0031/545; A61K-0031/522; A61K-0031/454; A61K-0031/557
	INCL	424085700; 424145100; 514171000; 514200000; 514012000; 514192000; 514263310; 514323000; 514573000
	IPCI	A61K0038-21 [ICM,7]; A61K0039-395 [ICS,7]; A61K0031-56 [ICS,7]; A61K0031-545 [ICS,7]; A61K0031-522 [ICS,7]; A61K0031-519 [ICS,7,C*]; A61K0031-454 [ICS,7]; A61K0031-4523 [ICS,7,C*]; A61K0031-557 [ICS,7]
	IPCR	A61K0031-4523 [I,C*]; A61K0031-454 [I,A]; A61K0031-519 [I,C*]; A61K0031-522 [I,A]; A61K0031-545 [I,A]; A61K0031-545 [I,C*]; A61K0031-557 [I,A]; A61K0031-557 [I,C*]; A61K0031-56 [I,A]; A61K0031-56 [I,C*]; A61K0038-18 [I,A]; A61K0038-18 [I,C*]; A61K0038-21 [I,A]; A61K0038-21 [I,C*]; A61K0038-27 [I,A]; A61K0038-27 [I,C*]
	NCL	424/085.700
	ECLA	A61K031/454; A61K031/522; A61K031/545; A61K031/557; A61K031/56; A61K038/18F+M; A61K038/21+M; A61K038/27+M
CA---2504263	IPCI	A61K0031-40 [ICM,7]; A61K0031-00 [ICS,7]
	IPCR	A61K0031-4523 [I,C*]; A61K0031-454 [I,A]; A61K0031-519 [I,C*]; A61K0031-522 [I,A]; A61K0031-545 [I,A]; A61K0031-545 [I,C*]; A61K0031-557 [I,A]; A61K0031-557 [I,C*]; A61K0031-56 [I,A]; A61K0031-56 [I,C*]; A61K0038-18 [I,A]; A61K0038-18 [I,C*]; A61K0038-21 [I,A]; A61K0038-21 [I,C*]; A61K0038-27 [I,A]; A61K0038-27 [I,C*]
	ECLA	A61K031/454; A61K031/522; A61K031/545; A61K031/557; A61K031/56; A61K038/18F+M; A61K038/21+M; A61K038/27+M
WO2004041181	IPCI	A61K [ICM,7]
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	ECLA	A61K031/454; A61K031/522; A61K031/545; A61K031/557; A61K031/56; A61K038/18F+M; A61K038/21+M; A61K038/27+M
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	ECLA	A61K031/454; A61K031/522; A61K031/545; A61K031/557; A61K031/56; A61K038/18F+M; A61K038/21+M; A61K038/27+M

[I,A]; A61K0038-21 [I,C*]; A61K0038-27 [I,A];
A61K0038-27 [I,C*]
EP---1567148 IPCI A61K0031-40 [ICM,7]; A61K0031-00 [ICS,7]
IPCR A61K0031-4523 [I,C*]; A61K0031-454 [I,A]; A61K0031-519
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A61K0031-545 [I,C*]; A61K0031-557 [I,A]; A61K0031-557
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A61K0038-18 [I,A]; A61K0038-18 [I,C*]; A61K0038-21
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ECLA A61K031/454; A61K031/522; A61K031/545; A61K031/557;
A61K031/56; A61K038/18F+M; A61K038/21+M; A61K038/27+M
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IPCR A61K0031-4523 [I,C*]; A61K0031-454 [I,A]; A61K0031-519
[I,C*]; A61K0031-522 [I,A]; A61K0031-545 [I,A];
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A61K0038-18 [I,A]; A61K0038-18 [I,C*]; A61K0038-21
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A61K0038-27 [I,C*]
CN---1731997 IPCI A61K0031-40 [I,A]; A61K0031-00 [I,A]
ECLA A61K031/454; A61K031/522; A61K031/545; A61K031/557;
A61K031/56; A61K038/18F+M; A61K038/21+M; A61K038/27+M
JP2006509743 IPCI A61K0045-00 [I,A]; A61K0031-4035 [I,A]; A61K0031-403
[I,C*]; A61K0031-409 [I,A]; A61K0031-454 [I,A];
A61K0031-4523 [I,C*]; A61K0045-06 [I,A]; A61P0009-00
[I,A]; A61P0009-10 [I,A]; A61P0027-02 [I,A];
A61P0027-00 [I,C*]
FTERM 4C084/AA17; 4C084/AA20; 4C084/MA02; 4C084/MA16;
4C084/MA66; 4C084/NA14; 4C084/ZA33; 4C084/ZA36;
4C084/ZC75; 4C086/AA01; 4C086/AA02; 4C086/BC10;
4C086/BC21; 4C086/CB04; 4C086/MA01; 4C086/MA02;
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4C086/ZC75
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A61K0031-522 [I,A]; A61K0031-545 [I,A]; A61K0031-557
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IPCR A61K0031-4523 [I,C*]; A61K0031-454 [I,A]; A61K0031-519
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A61K0031-545 [I,C*]; A61K0031-557 [I,A]; A61K0031-557
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A61K0038-18 [I,A]; A61K0038-18 [I,C*]; A61K0038-21
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IPCR A61K0031-4523 [I,C*]; A61K0031-454 [I,A]; A61K0031-519
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WO2005044269 IPCI A61K0031-445 [ICM,7]
IPCR A61K0031-4523 [I,C*]; A61K0031-454 [I,A]; A61K0031-519
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A61K0038-27 [I,C*]
ECLA A61K031/454; A61K031/522; A61K031/545; A61K031/557;
A61K031/56; A61K038/18F+M; A61K038/21+M; A61K038/27+M

OS MARPAT 140:386062

AB Methods of treating, preventing and/or managing macular degeneration are disclosed. Specific embodiments encompass the administration of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in combination with a second active agent and/or surgery. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed. Patients with macular degeneration were treated by photodynamic therapy with verteporfin alone, or with the addition of 20 mg/day of selective cytokine inhibitory drug (+)-2-[1-(3-ethoxy-4 methoxyphenyl)-2-methylsulfonylethyl]-4 acetylaminoisindoline 1,3-dione. The neovascular cascade is sufficiently hindered in the group receiving (+)-2-[1-(3-ethoxy-4 methoxyphenyl)-2-methylsulfonylethyl]-4 acetylaminoisindoline 1,3-dione to indefinitely prolong the effects of the photodynamic therapy.

ST selective cytokine inhibitory drug management macular degeneration

IT Eye, disease
(Behr's disease, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Eye, disease
(Doyne's disease, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Eye, disease
(Sorsby's disease, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Steroids, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(angiostatic, as second active agent, in combination; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Angiogenesis inhibitors
Anti-inflammatory agents
Antibiotics
Antioxidants
Photosensitizers, pharmaceutical
(as second active agent, in combination; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Integrins
Interferons
Neurotrophic factors
Phytoestrogens
Prostaglandins
Steroids, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as second active agent, in combination; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Eye, disease
(atrophy of retinal pigment epithelium, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Eye
(foveal translocation; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Eye, disease
(fundus flavimaculatus, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Eye, disease
(honeycomb dystrophy, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Drugs
Surgery
(in combination; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Tumor necrosis factors

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)

(inhibition of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

- IT Eye, disease
(macula, degeneration, Stargardt's disease, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
- IT Eye, disease
(macula, degeneration, congenital, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
- IT Eye, disease
(macula, degeneration; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
- IT Eye, disease
(macula, senile degeneration, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
- IT Eye, disease
(macular damage, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
- IT Eye, disease
(macular dystrophy, juvenile, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
- IT Eye, disease
(maculopathy, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
- IT Angiogenesis
(neovascularization, eye, regulator of, as second active agent, in combination; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
- IT Eye, disease
(neovascularization, regulator of, as second active agent, in combination; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
- IT Angiogenesis
(neovascularization, retinal, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
- IT Solvates
Stereoisomers
(of selective cytokine inhibitory drugs; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
- IT Clathrates
Hydrates
Salts, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(of selective cytokine inhibitory drugs; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
- IT Eye
(pigment epithelium, detachment or atrophy of, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
- IT Drug delivery systems
(prodrugs, of selective cytokine inhibitory drugs; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
- IT Eye, disease
(retina, detachment, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)
- IT Eye, disease
(retina, neovascularization, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular

degeneration)

IT Eye
(retinal pigment epithelium transplant; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Transplant and Transplantation
(retinal pigment epithelium; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Epithelium
(retinal pigment, detachment or atrophy of, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Drug delivery systems
Human
Phototherapy
Radiotherapy
(selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Cytokines
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(selective inhibitors; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Lasers
(therapy; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(to VEGF, as second active agent, in combination; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Eye, disease
(vitelliform, treatment of; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT Interferons
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
($\alpha 2$, as second active agent, in combination; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT 127464-60-2, Vascular endothelial growth factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antibody to, as second active agent, in combination; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT 50-35-1, Thalidomide 69-89-6D, Xanthine, derivs. 6493-05-6, Pentoxifylline 9002-72-6, Growth hormone 129497-78-5, Verteporfin 284041-10-7, Purlitin 688035-40-7, RhuFab
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as second active agent, in combination; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

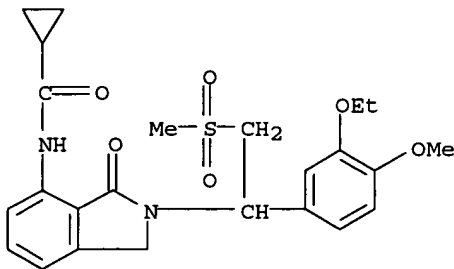
IT 167886-76-2 167886-76-2D, salts, solvates, stereoisomers 340019-67-2 340019-67-2D, salts, solvates, stereoisomers 608141-41-9
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

IT 127464-60-2, Vascular endothelial growth factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antibody to, as second active agent, in combination; selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

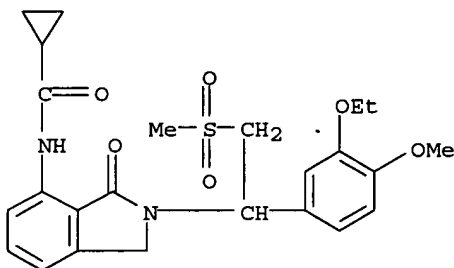
RN 127464-60-2 HCAPLUS
CN Vascular endothelial growth factor (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 340019-67-2 340019-67-2D, salts, solvates, stereoisomers
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
 THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (selective cytokine inhibitory drugs and compns. for treatment and
 management of macular degeneration)
 RN 340019-67-2 HCAPLUS
 CN Cyclopropanecarboxamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)-2-(
 (methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA
 INDEX NAME)



RN 340019-67-2 HCAPLUS
 CN Cyclopropanecarboxamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)-2-(
 (methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA
 INDEX NAME)



L17 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
 AN 2003:1001604 HCAPLUS
 DN 140:42030
 ED Entered STN: 24 Dec 2003
 TI Preparation of isoindolinediones as angiogenesis inhibitors.
 IN Man, Hon-wah; Muller, George W.
 PA Celgene Corporation, USA
 SO U.S., 28 pp., Cont.-in-part of U.S. Ser. No. 590,344.
 CODEN: USXXAM
 DT Patent
 LA English
 IC ICM C07D-0413/04
 ICS C07D-0403/04; C07D-0235/16; A61K-0031/4184; A61P-0035/00
 INCL 514323000; 514383000; 514385000; 514412000; 514416000; 514417000;
 546143000; 546266400; 546312100; 546466000
 CC 27-11 (Heterocyclic Compounds (One Hetero Atom))
 Section cross-reference(s): 1, 63
 FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	US---6667316	B1	20031223	2000US-0708199	20001108
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CLASS

PATENT NO.

CLASS

PATENT FAMILY CLASSIFICATION CODES

US 6667316

ICM

C07D-0413/04

ICS

C07D-0403/04; C07D-0235/16; A61K-0031/4184; A61P-0035/00

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514/323.000; 514/383.000; 514/385.000; 514/412.000; 514/416.000; 514/417.000; 546/143.000

ECLA

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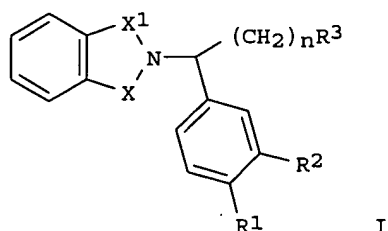
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AB Title compds. [I; R1, R2 = alkyl, alkoxy, cyano, cycloalkoxy, cycloalkyl, cycloalkylmethoxy; 1 of X and X1 = CO, SO2 and the other of X and X1 = CO, CH2, SO2, CH2CO; R3 = SO2Y, COZ, CN; hydroxyalkyl; Y = alkyl, Ph, PhCH2; Z = NR61R71, alkyl, Ph, PhCH2; R61 = H, alkyl, cycloalkyl, Ph, PhCH2, etc.; R71 = alkyl; 1 of R4, R5 = H and the other = imidazolyl, pyrrolyl, oxadiazolyl, triazolyl, R6R7N(CzH2z); z = 0, 1; n = 1-3; R6 = cycloalkanoyl which is unsubstituted or substituted with halo, amino, monoalkylamino, dialkylamino; R4R5 = NHCH2R8, NHCOR8, N:CHR8; R7 = H, alkyl, methylsulfonyl, alkoxyalkylcarbonyl; R8 = CH2, O, NH, CH:CH, CH:N], were prepared for treatment of undesirable angiogenesis (no data). Thus, 3,4-dinitrophthalic acid and 2-(3-ethoxy-4-methoxyphenyl)-1-(methylsulfonyl)eth-2-ylamine in PhMe were refluxed for 15 h through a Dean-Stark trap to give 49% 2-[1-(3-Ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4,5-dinitroisoindoline-1,3-dione. This was hydrogenated in EtOAc over Pd/C to give 73% 2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4,5-diaminoisoindoline-1,3-dione. The latter was refluxed 17 h with DMF di-Me acetal in HOAc to give 68% 7-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-3-pyrrolino[3,4-e]benzimidazole-6,8-dione.

ST isoindolinedione prepn angiogenesis inhibitor

IT Angiogenesis

Angiogenesis inhibitors

Human

(preparation of isoindolinediones as angiogenesis inhibitors)

IT 340019-32-1P 340019-79-6P 340019-81-0P
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of isoindolinediones as angiogenesis inhibitors)

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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
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(preparation of isoindolinediones as angiogenesis inhibitors)

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RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of isoindolinediones as angiogenesis inhibitors)

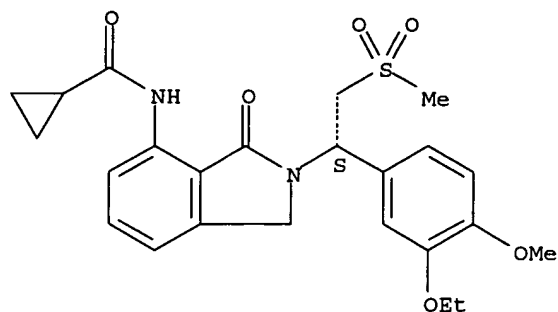
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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
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(preparation of isoindolinediones as angiogenesis inhibitors)

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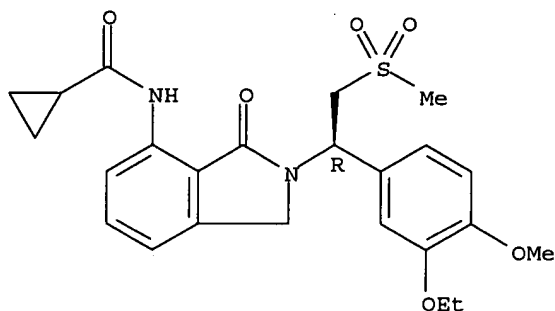
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RN 340019-70-7 HCAPLUS

CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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FILE 'USPATFULL' ENTERED AT 08:45:58 ON 20 JUL 2006

CA INDEXING COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 08:45:58 ON 20 JUL 2006

CA INDEXING COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

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L22 ANSWER 1 OF 2 USPATFULL on STN

AN 2004:120049 USPATFULL

TI Methods of using and compositions comprising selective cytokine inhibitory drugs for treatment and management of macular degeneration

IN Zeldis, Jerome B., Princeton, NJ, UNITED STATES

PI US2004091454 A1 20040513

AI 2003US-0699110 A1 20031030 (10)

PRAI 2002US-422900P 20021031 (60)

DT Utility

FS APPLICATION

LREP JONES DAY, 222 EAST 41ST STREET, NEW YORK, NY, 10017

CLMN Number of Claims: 22

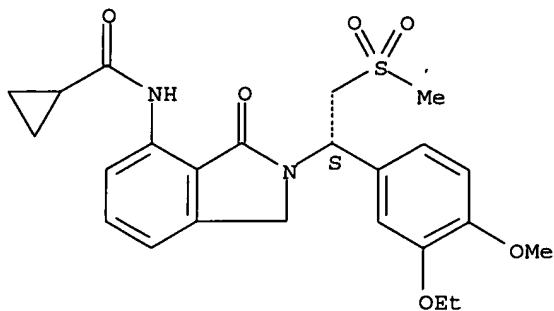
ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1771

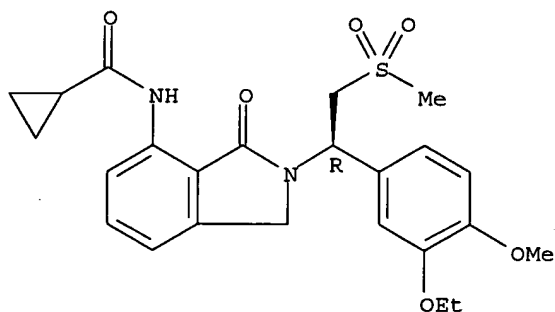
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods of treating, preventing and/or managing macular degeneration are disclosed. Specific embodiments encompass the administration of a selective cytokine inhibitory drug, or a pharmaceutically acceptable



RN 340019-70-7 HCAPLUS
 CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L17 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
 AN 2001:359998 HCAPLUS
 DN 134:366799
 ED Entered STN: 18 May 2001
 TI Preparation of isoindolinones for treatment of phosphodiesterase- and TNF α -mediated diseases
 IN Man, Hon-Wah; Muller, George
 PA Celgene Corporation, USA
 SO PCT Int. Appl., 94 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM C07D-0487/04
 ICS C07D-0471/04; C07D-0413/04; C07D-0403/04; C07D-0209/46; C07D-0209/48; C07D-0209/49; A61K-0031/4188; A61K-0031/437; A61K-0031/4985; A61K-0031/4245; A61K-0031/4196; A61K-0031/4178; A61K-0031/4035; A61P-0011/06
 CC 27-11 (Heterocyclic Compounds (One Hetero Atom))
 Section cross-reference(s): 1

FAN.CNT 4

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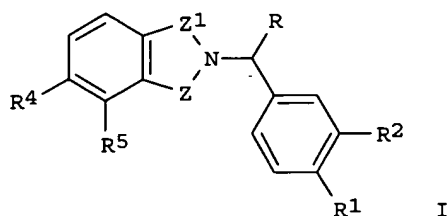
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 2000US-0590344 A 20000608
 2000US-0708199 A 20001108
 2000WO-US30770 W 20001109

CLASS

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 OS MARPAT 134:366799
 GI



AB Title compds. [I; R = (C_nH_{2n})R₃; R₁,R₂ = (cyclo)alkyl(oxy), cyano, cycloalkylmethoxy; R₃ = hydroxyalkyl, cyano, SO₂R₆, COR₇; 1 of R₄,R₅ = H and the other = pyrrolyl, imidazolyl, (un)substituted amino(alkyl), etc.; R₄,R₅ = (un)substituted amino(alkyl); R₄R₅ = atoms to complete a ring; R₆ = alkyl, Ph, CH₂Ph; R₇ = groups cited for R₆, (un)substituted amino; 1 of Z,Z₁ = CO or SO₂ and the other = CH₂, CO, SO₂, CH₂CO; n = 1-3] were prepared for treatment of phosphodiesterase- and TNF α -mediated diseases (no data). Thus, 3,4-dinitrophthalic acid was cyclocondensed with H₂NCH(CH₂SO₂Me)C₆H₃(OEt)(OMe)-3,4 and the product reduced to give I (R = CH₂SO₂Me, R₁ = OMe, R₂ = OEt, R₄ = R₅ = NH₂, Z = Z₁ = CO).

ST isoindolinones prepn treatment phosphodiesterase TNF α mediated disease

IT Angiogenesis inhibitors

Antitumor agents

(preparation of isoindolinones for treatment of phosphodiesterase- and TNF α -mediated diseases)

IT Tumor necrosis factors

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(preparation of isoindolinones for treatment of phosphodiesterase- and TNF α -mediated diseases)

IT 340019-17-2P 340019-23-0P 340019-32-1P 340019-39-8P 340019-43-4P
340019-46-7P 340019-48-9P 340019-51-4P 340019-53-6P 340019-81-0P
340019-83-2P 340019-87-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of isoindolinones for treatment of phosphodiesterase- and TNF α -mediated diseases)

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340019-84-3P 340019-85-4P 340019-86-5P 340019-88-7P 340019-89-8P
340019-90-1P 340019-95-6P 340019-96-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of isoindolinones for treatment of phosphodiesterase- and TNF α -mediated diseases)

IT 9036-21-9, Phosphodiesterase-IV 141907-41-7, Matrix Metalloproteinase

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(preparation of isoindolinones for treatment of phosphodiesterase- and TNF α -mediated diseases)

IT 696-59-3, 2,5-Dimethoxytetrahydrofuran 4023-34-1, Cyclopropanecarbonyl chloride 4524-93-0, Cyclopentanecarbonyl chloride 6296-53-3, 3-Acetamidophthalic anhydride 7148-74-5, 2-Bromopropionyl chloride

15486-96-1, 3-Bromopropionyl chloride 92971-15-8, 3,4-Dinitrophthalic acid 143092-07-3, Furo[3,4-h]quinoline-7,9-dione 201408-36-8
 253168-83-1 253168-94-4 340019-97-8 340019-98-9 340019-99-0
 340020-00-0 340020-01-1 340020-02-2, 3-Amino-N-ethoxycarbonylphthalimide 340020-03-3 340020-04-4 340020-05-5
 340020-06-6 340020-07-7 340020-08-8

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of isoindolinones for treatment of phosphodiesterase- and TNF α -mediated diseases)

IT 340019-16-1P 340019-34-3P 340019-35-4P 340019-36-5P 340019-37-6P
 340019-38-7P 340019-91-2P 340019-92-3P 340019-93-4P 340019-94-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of isoindolinones for treatment of phosphodiesterase- and TNF α -mediated diseases)

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Duplantier, A; 7-Oxo-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridines as Novel Inhibitors of Human Eosinophil Phosphodiesterase 1998, V41(13); P2268 HCAPLUS
- (2) Giembycz, M; Drugs 2000, V59(2), P193 HCAPLUS
- (3) He, W; Novel Cyclic Compounds as potent Phosphodiesterase 4 Inhibitors 1998, V41(22), P4216 HCAPLUS
- (4) Muller, G; Bioorg Med Chem Let 1998, V8, P2669 HCAPLUS
- (5) Muller, G; J Med Chem 1996, V39, P3238 HCAPLUS

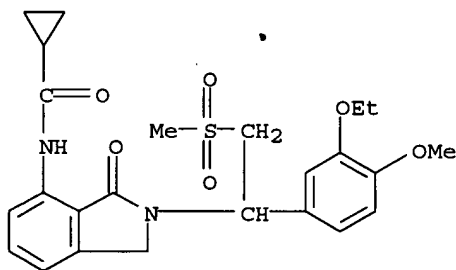
IT 340019-67-2P 340019-69-4P 340019-70-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of isoindolinones for treatment of phosphodiesterase- and TNF α -mediated diseases)

RN 340019-67-2 HCAPLUS

CN Cyclopropanecarboxamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

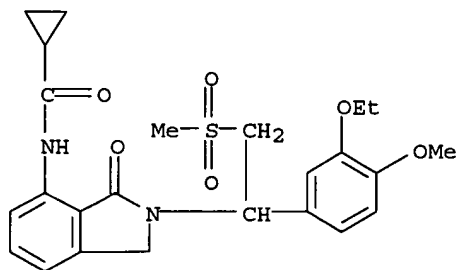


RN 340019-69-4 HCAPLUS

CN Cyclopropanecarboxamide, N-[2-[(1S)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

- (33) Muller; US---5703098 A 1997 HCAPLUS
 (34) Muller; US---5728844 A 1998 HCAPLUS
 (35) Muller; US---5728845 A 1998 HCAPLUS
 (36) Muller; US---5736570 A 1998 HCAPLUS
 (37) Muller; US---5801195 A 1998 HCAPLUS
 (38) Muller; US---5877200 A 1999 HCAPLUS
 (39) Muller; US---5929117 A 1999 HCAPLUS
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 (43) Muller; US---6046221 A 2000 HCAPLUS
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 (63) Tracey, K; Annu Rev Cell Biol 1993, V9, P317 HCAPLUS
 (64) Wojtowicz-Praga, S; Investigational New Drugs 1997, V15, P61 HCAPLUS
 (65) Yu, A; Drugs & Aging 1997, V11(3), P229 HCAPLUS
 IT 340019-67-2P 340019-69-4P 340019-70-7P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of isoindolinediones as angiogenesis inhibitors)
 RN 340019-67-2 HCAPLUS
 CN Cyclopropanecarboxamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)



- RN 340019-69-4 HCAPLUS
 CN Cyclopropanecarboxamide, N-[2-[(1S)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in combination with a second active agent and/or surgery. Pharmaceutical compositions, single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed.

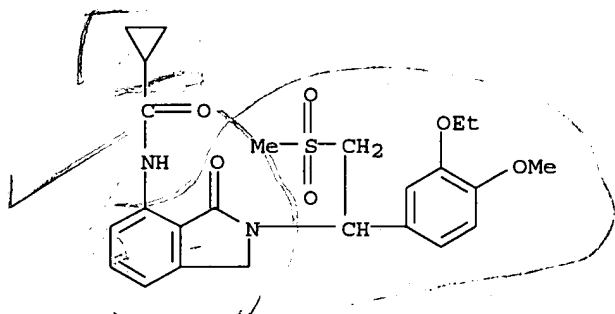
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 340019-67-2 340019-67-2D, salts, solvates, stereoisomers

(selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

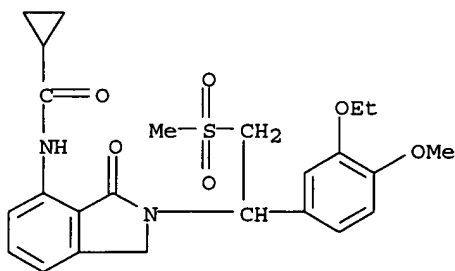
RN 340019-67-2 USPATFULL

CN Cyclopropanecarboxamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)



RN 340019-67-2 USPATFULL

CN Cyclopropanecarboxamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)



L22 ANSWER 2 OF 2 USPATFULL on STN

AN 2003:332383 USPATFULL

TI Pharmaceutically active isoindoline derivatives

IN Man, Hon-Wah, Princeton, NJ, United States

Muller, George W, Bridgewater, NJ, United States

PA Celgene Corporation, Warren, NJ, United States (U.S. corporation)

PI US---6667316 B1 20031223

AI 2000US-0708199 20001108 (9)

RLI Continuation-in-part of Ser. No. 2000US-0590344, filed on 8 Jun 2000

PRAI 1999US-165168P 19991112 (60)

DT Utility

FS GRANTED

EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: McKenzie, Thomas

LREP Mathews, Collins, Shepherd & McKay, P.A.

CLMN Number of Claims: 19

ECL Exemplary Claim: 1

DRWN 0 Drawing Figure(s); 0 Drawing Page(s)

LN.CNT 2999

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A compound of formula I wherein each of R.sup.1 and R.sup.2, independently of the other, is alkyl, alkoxy, cyano, cycloalkoxy, cycloalkyl or cycloalkylmethoxy; one of X and X' is .dbd.C.dbd.O or .dbd.SO.sub.2 and the other of X and X' is a divalent group selected from .dbd.C.dbd.O, .dbd.CH.sub.2, .dbd.SO.sub.2 or .dbd.CH.sub.2C.dbd.O; R.sup.3 is --SO.sub.2--Y, --COZ, --CN, or hydroxyalkyl in which Y is alkyl, phenyl, or benzyl and Z is --NR.sup.6"R.sup.7", alkyl, phenyl, or benzyl; one of R.sup.4 and R.sup.5 is hydrogen and the other of R.sup.4 and R.sup.5 is imidazolyl, pyrrolyl, oxadiazolyl, triazolyl, or R.sup.6R.sup.7N(C.sub.zH.sub.2z)-- wherein R.sup.6, when taken independently of R.sup.7, is cycloalkanoyl which is unsubstituted or substituted with halo, amino, monoalkylamino or dialkylamino; and R.sup.7 is hydrogen, alkyl of 1 to 4 carbon atoms, methylsulfonyl; or alkoxyalkylcarbonyl. Compounds of the present invention are useful as inhibitors of TNF α , PDE 4, matrix metalloproteases, and angiogenesis, and for treating cancer, autoimmune disease, and inflammatory disease. ##STR1##

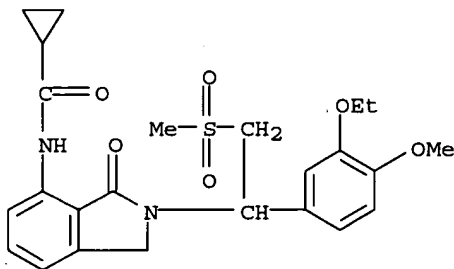
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 340019-67-2P 340019-69-4P 340019-70-7P

(preparation of isoindolinones as angiogenesis inhibitors)

RN 340019-67-2 USPATFULL

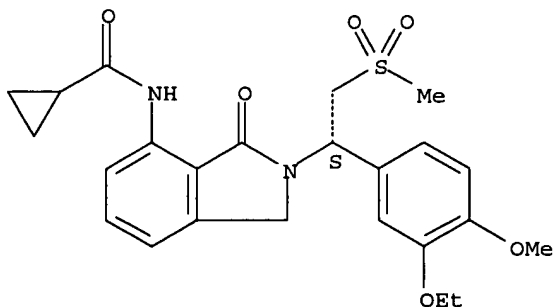
CN Cyclopropanecarboxamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)



RN 340019-69-4 USPATFULL

CN Cyclopropanecarboxamide, N-[2-[(1S)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

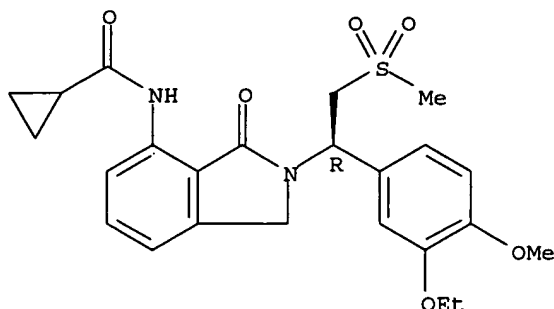


RN 340019-70-7 USPATFULL

CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

INDEX NAME)

Absolute stereochemistry.



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<http://scientific.thomson.com/media/scpdf/ipcrdwpf.pdf> <<<

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http://www.stn-international.de/stdatabases/details/dwpi_r.html <<<
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L42 ANSWER 1 OF 5 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN

AN 2005-746262 [76] WPIX

DNC C2005-227366

TI Use of phosphodiesterase-4 modulators for treatment, prevention, or
 managing pulmonary hypertension and associated symptoms.

DC B03 B05

IN ZELDIS, J B

PA (ZELD-I) ZELDIS J B; (CELG-N) CELGENE CORP

CYC 110

PI US--2005239867 A1 20051027 (200576)* 33 A61K-031-704

WO--2005102317 A1 20051103 (200576) EN A61K-031-40

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IS IT
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 ZM ZW

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 NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SM SY TJ TM TN TR TT TZ
 UA UG US UZ VC VN YU ZA ZM ZW

ADT US--2005239867 A1 Provisional 2004US-565174P 20040423, 2005US-0111187

20050421; WO--2005102317 A1 2005WO-US13597 20050421
 PRAI 2004US-565174P 20040423; 2005US-0111187 20050421
 IC ICM A61K-031-40; A61K-031-704
 ICS A61K-031-366; A61K-031-397; A61K-031-4035; A61K-031-519
 AB US2005239867 A UPAB: 20051125

NOVELTY - Treatment, prevention, or managing pulmonary hypertension involves administration of phosphodiesterase-4 (PDE-4) modulator, its salt, solvate or stereoisomer.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a pharmaceutical composition comprising the PDE4 modulator, its salt, solvate or stereoisomer, and a second active agent capable of reducing pulmonary artery pressure or a symptom of pulmonary hypertension.

ACTIVITY - Hypotensive; Respiratory-Gen.; Cardiovascular-Gen.; Analgesic; Muscular-Gen.; Immunomodulator; Antiinflammatory; Cerebroprotective; Hypertensive; Anticonvulsant; Cardiant; CNS-Gen.

Efficacy of 3-(3,4-dimethoxy-phenyl)-3-(1-oxo-1,3-dihydro-isoindol-2-yl)-propionamide (Ia) was evaluated in patients with pulmonary hypertension for 12 weeks. (Ia) was administered at dosage of 1 - 1200 mg/day, and the patients were evaluated for decline in walk distance, dyspnea score, and pulmonary hemodynamic response. The patients treated with (Ia) showed improvement in dyspnea score as compared to placebo-treated patients (control). Also the patients treated with (Ia) walked approx. 70 meters farther after 12 weeks while the control group of the patients showed decline in walk distance; and there was decrease in pulmonary arterial pressure and pulmonary vascular resistance, and increase in cardiac output as compared to worsening of pulmonary hemodynamics in control group.

MECHANISM OF ACTION - PDE4 (phosphodiesterase) modulator; Selective cytokine inhibitor.

USE - For treating, prevention and managing primary and secondary pulmonary hypertension (e.g. of functional classes I - IV) before, during or after surgery or lung transplantation; and also for treating symptoms associated with pulmonary hypertension (claimed) including dyspnea, fatigue, weakness, chest pain, recurrent syncope, seizures, light-headedness, leg edema and palpitations.

ADVANTAGE - The PDE4 modulators are enantiomerically pure, and exhibit selective cytokine inhibitory activities (e.g. inhibit inflammatory cytokines such as tumor necrosis- alpha production in monocytes as well as in lymphocytes); exhibit excellent immunomodulatory activities that may provide additive or synergistic effect when given before, concurrently with, or after surgery or transplantation therapy; reduce complications associated with the transplantation as well as adverse side effects than the prior art therapies; improve exercise capacity; and provide safe and effective treatment and management therapy for pulmonary hypertension.

Dwg. 0/0

FS CPI

FA AB; GI; DCN

MC CPI: B01-D02; B05-C03; B06-H; B07-H; B10-A17; B10-C03; B10-C04A; B10-E04A; B14-C01; B14-C03; B14-D07A1; B14-D07C; B14-E11; B14-F01A; B14-F02; B14-F04; B14-F06; B14-F07; B14-J01A2; B14-J05; B14-J07; B14-K01; B14-L01; B14-L04; B14-L06; B14-N08

M2 *01* DCN: R11504-M; R11504-K

M2 *02* DCN: R04284-M; R04284-K; R07098-M; R07098-K

M2 *03* DCN: R03027-M; R03027-K; R11668-M; R11668-K

M2 *04* DCN: R03935-M; R03935-K

M2 *05* DCN: RA4IB0-M; RA4IB0-K

M2 *06* DCN: RA0WC2-M; RA0WC2-K

M2 *07* DCN: R00487-M; R00487-K; R14664-M; R14664-K

M2 *08* DCN: RA2HIY-M; RA2HIY-K

M2 *09* DCN: R16884-M; R16884-K

M2 *10* DCN: RA0GH5-M; RA0GH5-K

M2 *11* DCN: RA00K2-M; RA00K2-K

M2 *12* DCN: R18645-M; R18645-K

M2 *13* DCN: R01901-M; R01901-K

M2 *14* DCN: R04093-M; R04093-K; R04742-M; R04742-K

M2 *15* DCN: R06894-M; R06894-K
 M2 *16* DCN: R18629-M; R18629-K
 M2 *17* DCN: RA05WZ-M; RA05WZ-K; RA6YW3-M; RA6YW3-K
 M2 *19* DCN: RAK0A8-M; RAK0A8-U; RAK0A8-K
 M2 *20* DCN: RA4TIW-M; RA4TIW-U; RA4TIW-K
 M2 *21* DCN: RAK0A9-M; RAK0A9-U; RAK0A9-K
 M2 *22* DCN: RAK0AA-M; RAK0AA-U; RAK0AA-K
 M2 *23* DCN: RAK0AB-M; RAK0AB-U; RAK0AB-K
 M2 *24* DCN: RAK0AC-M; RAK0AC-U; RAK0AC-K
 M2 *25* DCN: RAK0AD-M; RAK0AD-U; RAK0AD-K
 M2 *26* DCN: 0208-65801-M; 0208-65801-U; 0208-65801-K
 M2 *27* DCN: 0208-65802-M; 0208-65802-U; 0208-65802-K
 M5 *18* DCN: R02018-M; R02018-K

DCRE 87314-0-0-0; 69325-1-0-0; 6754-0-0-0; 94351-1-0-0; 86001-1-0-0;
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ABEX UPTX: 20051125

SPECIFIC COMPOUNDS - Use of 7 compounds as the PDE-4 modulator, e.g.
 3-(3,4-dimethoxy-phenyl)-3-(1-oxo-1,3-dihydro-isoindol-2-yl)-propionamide,
 cyclopropanecarboxylic acid (2-(1-(3-ethoxy-4-methoxy-phenyl)-2-
 methanesulfonyl-ethyl)-3-oxo-2,3-dihydro-1H-isoindol-4-yl)-amide, and
 4-(1-aza-2-(dimethylamino)prop-1-enyl)-2-(1-(3-ethoxy-4-methoxyphenyl)-2-
 methylsulfonylethyl)isoindoline-1,3-dione is specifically claimed.

ADMINISTRATION - Dosage of the PDE4 modulator is 1 - 10000 (preferably 1 - 2500, especially 1 - 20) mg/day; and that of the second agent is 1 - 1000 (preferably 50 - 200) mg. Administration is by oral, mucosal (e.g. nasal, sublingual, vaginal, buccal or rectal), or parenteral (e.g. subcutaneous, intravenous, intramuscular or intraarterial) route, or by inhalation.

TECH UPTX: 20051125

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: The PDE4 modulator is a cyclic amide derivative of formula (I) or imido and amido substituted alkanohydroxamic acids of formula (II).

n=1 - 3;

R5=o-phenylene (optionally mono- - tetra-substituted by nitro, cyano, trifluoromethyl, carboethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkylamino, dialkylamino, acylamino, 1-10C alkyl, or halo);

R7=phenyl (optionally substituted with at least one of T1), benzyl (optionally mono- - tri-substituted by T1), naphthyl, or benzyloxy;

T1=nitro, cyano, trifluoromethyl, carboethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, 1-10C alkyl, 1-10C alkoxy, or halo;

R12=OH, 1-12C alkoxy, or -NR8R9;

R8=H or 1-10C alkyl;

R9=H, 1-10C alkyl, COR10, or -SO2R10;

R10=H, 1-10C alkyl, or phenyl;

R1 and R2=H or lower alkyl;

CR1+CR2=o-phenylene, o-naphthylene, or cyclohexene-1,2-diyl (all optionally mono- - tetra-substituted by nitro, cyano, trifluoromethyl, carboethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkylamino, dialkylamino, acylamino, 1-10C alkyl, 1-10C alkoxy, or halo);

R3=phenyl (mono- - tetra-substituted by nitro, cyano, trifluoromethyl, carboethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, 1-10C alkyl, 1-10C alkoxy, 1-10C alkylthio, benzyloxy, 3-6C cycloalkoxy, 4-6C cycloalkylidenemethyl, 3-10C alkylidenemethyl, indanyloxy, or halo);

R4=H, 1-6C alkyl, phenyl, or benzyl;

R4a=H or 1-6C alkyl;

R5a=-CH2-, -CH2-CO-, -SO2-, -S-, or -NHCO-;

m=0 - 2.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method: The method further involves administration of a second active agent that is capable of

reducing pulmonary artery pressure or symptoms of the pulmonary hypertension. Preferred Components: The second active agent is anticoagulant, diuretic, cardiac glycoside, calcium channel blocker, vasodilator, prostacyclin analogue, endothelin antagonist, phosphodiesterase inhibitor, endopeptidase inhibitor, lipid lowering agent, or a thromboxane inhibitor (preferably amlodipine, diltiazem, nifedipine, epoprostenol, treprostinil, bosentan, warfarin, tadalafil, simvastatin, omapatrilat, irbesartan, pravastatin, digoxin, nitric oxide, L-arginine, iloprost, betaprost, or sildenafil).

L42 ANSWER 2 OF 5 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
 AN 2004-420074 [39] WPIX
 CR 2004-034763 [03]; 2004-034766 [03]; 2004-420073 [39]; 2005-031046 [03]
 DNC C2004-157704
 TI Use of a cytokine inhibitory drug to treat, manage or prevent e.g. cancer and diseases associated with undesired angiogenesis.
 DC B05
 IN ZELDIS, J B
 PA (CELG-N) CELGENE CORP; (ZELD-I) ZELDIS J B
 CYC 108
 PI WO--2004043378 A2 20040527 (200439)* EN 74 A61K-000-00
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 LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
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 AU--2003290652 A1 20040603 (200470) A61K-000-00
 EP-----1567154 A2 20050831 (200561) EN A61K-031-44
 R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV
 MC MK NL PT RO SE SI SK TR
 BR---200316057 A 20050920 (200566) A61K-031-44
 US--2006035955 A1 20060216 (200613) A61K-031-403
 JP--2006508131 W 20060309 (200620) 61 A61K-045-00
 MX--2005004780 A1 20051001 (200620) A61K-031-40
 KR--2005072802 A 20050712 (200643) A61K-031-44
 ADT WO--2004043378 A2 2003WO-US035545 20031106; AU--2003290652 A1
 2003AU-0290652 20031106; EP-----1567154 A2 2003EP-0783234 20031106,
 2003WO-US35545 20031106; BR---200316057 A 2003BR-0016057 20031106,
 2003WO-US35545 20031106; US--2006035955 A1 2003WO-US35545 20031106,
 2005US-0534325 20050912; JP--2006508131 W 2003WO-US35545 20031106,
 2004JP-0551873 20031106; MX--2005004780 A1 2003WO-US35545 20031106,
 2005MX-0004780 20050504; KR--2005072802 A 2003WO-US35545 20031106,
 2005KR-0708122 20050506
 FDT AU--2003290652 A1 Based on WO--2004043378; EP-----1567154 A2 Based on
 WO--2004043378; BR---200316057 A Based on WO--2004043378; JP--2006508131 W
 Based on WO--2004043378; MX--2005004780 A1 Based on WO--2004043378;
 KR--2005072802 A Based on WO--2004043378
 PRAI 2002US-424601P 20021106; 2005US-0534325 20050912
 IC ICM A61K-000-00; A61K-031-40; A61K-031-403; A61K-031-4035; A61K-031-44;
 A61K-045-00
 ICS A61K-031-415; A61K-031-425; A61K-031-519; A61K-031-522; A61K-038-19;
 A61P-035-00; A61P-043-00
 AB WO2004043378 A UPAB: 20060706
 NOVELTY - Treatment, management or prevention of a specific cancer,
 comprises administration of a therapeutically or prophylactically
 effective amount of a selective cytokine inhibitory drug (I) or a salt,
 solvate or stereoisomer.
 DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
 (1) a method of treating, managing or preventing a disease associated
 with undesired angiogenesis, comprising administration of (I);
 (2) a method for reducing or avoiding an adverse effect associated
 with radiation therapy, hormonal therapy, biological therapy or
 immunotherapy and with administration of a second active ingredient (IV)
 in a patient suffering from cancer, comprises administration of (I);

(3) a method of treating, preventing or managing a specific cancer that is refractory to conventional therapy, which comprises administering (I) or a salt, solvate or stereoisomer and (IV) and transplanting umbilical cord blood, placental blood, peripheral blood stem cell, hematopoietic stem cell preparation or bone marrow in the patient;

(4) a pharmaceutical composition (A) comprising (I) or a salt, solvate or stereoisomer and (IV);

(5) a kit comprising a pharmaceutical composition (B) comprising (I) or a salt, solvate or stereoisomer and a pharmaceutical composition (C) comprising (IV); and

(6) a kit comprising (B) and umbilical cord blood, placental blood, peripheral blood stem cell, hematopoietic stem cell preparation or bone marrow.

ACTIVITY - Cytostatic; Anti-HIV; Dermatological; Vasotropic; Antidiabetic; Ophthalmological; Immunosuppressive; Antiinflammatory; Antiseborrheic; Antibacterial; Antilipemic; Antiulcer; Fungicide; Virucide; Auditory; Protozoacide; Antiarthritic; Antirheumatic; Tranquilizer; Vulnerary; Antianemic; Antisickling; Osteopathic; Cardiovascular-Gen.; CNS-Gen.; Gastrointestinal-Gen.; Cerebroprotective; Antiangiogenic.

MECHANISM OF ACTION - Cytokine inhibitor. Test details are described for cytokine inhibitory activity but no results given.

USE - (I) are useful for reducing or avoiding an adverse effect associated with the administration of (IV) and for treating, managing or preventing a specific cancer or a cancer that is refractory to conventional therapy (advanced malignancy, amyloidosis, neuroblastoma, meningioma, hemangiopericytoma, multiple brain metastase, glioblastoma multiforms, glioblastoma, brain stem glioma, poor prognosis malignant brain tumor, malignant glioma, anaplastic astrocytoma, anaplastic oligodendroglioma, neuroendocrine tumor, rectal adenocarcinoma, Dukes C and D colorectal cancer, unresectable colorectal carcinoma, metastatic hepatocellular carcinoma, Kaposi's sarcoma, karotype acute myeloblastic leukemia, Hodgkin's lymphoma, non-Hodgkin's lymphoma, cutaneous T-Cell lymphoma, cutaneous B-Cell lymphoma, diffuse large B-Cell lymphoma, low grade follicular lymphoma, metastatic melanoma, localized melanoma, malignant mesothelioma, malignant pleural effusion mesothelioma syndrome, peritoneal carcinoma, papillary serous carcinoma, gynecologic sarcoma, soft tissue sarcoma, scleroderma, cutaneous vasculitis, Langerhans cell histiocytosis, leiomyosarcoma, fibrodysplasia ossificans progressive, hormone refractory prostate cancer, resected high-risk soft tissue sarcoma, unrescectable hepatocellular carcinoma, Waldenstrom's macroglobulinemia, smoldering myeloma, indolent myeloma, fallopian tube cancer, androgen independent prostate cancer, androgen dependent stage IV non-metastatic prostate cancer, hormone-insensitive prostate cancer, chemotherapy-insensitive prostate cancer, papillary thyroid carcinoma, follicular thyroid carcinoma, medullary thyroid carcinoma or leiomyoma) and a disease (diabetic retinopathy, retinopathy of prematurity, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, proliferative vitreoretinopathy, trachoma, myopia, optic pits, epidemic keratoconjunctivitis, atopic keratitis, superior limbic keratitis, pterygium keratitis sicca, sjogrens, acne rosacea, phlyctenulosis, syphilis, lipid degeneration, bacterial ulcer, fungal ulcer, Herpes simplex infection, Herpes zoster infection, protozoan infection, Mooren ulcer, Terrien's marginal degeneration, mariginal keratolysis, rheumatoid arthritis, systemic lupus, polyarteritis, trauma, Wegeners sarcoidosis, Scleritis, Steven's Johnson disease, periphigoid radial keratotomy, sickle cell anemia, sarcoid, pseudoxanthoma elasticum, Paget's disease, vein occlusion, artery occlusion, carotid obstructive disease, chronic uveitis, chronic vitritis, Lyme's disease, Eales disease, Bechet's disease, retinitis, choroiditis, presumed ocular histoplasmosis, Bests disease, Stargarts disease, pars planitis, chronic retinal detachment, hyperviscosity syndromes, toxoplasmosis, sclerosing cholangitis, rubeosis, endotoxemia, toxic shock syndrome, osteoarthritis, retrovirus replication, wasting, meningitis, silica-induced fibrosis, asbestos-induced fibrosis, veterinary disorder, malignancy-associated hypercalcemia, stroke, circulatory shock, periodontitis, gingivitis, macrocytic anemia,

refractory anemia or 5q-syndrome) associated with undesired angiogenesis (all claimed).

ADVANTAGE - (I) reduces adverse side effects.

Dwg.0/0

FS

CPI

FA

AB; GI; DCN

MC

CPI: B01-B02; B02-D; B03-A; B04-A06; B04-B03A; B04-B03C; B04-B04D; B04-B04E; B04-F02; B04-H02B; B04-H04A; B04-H04C; B04-H05; B04-N06; B06-H; B07-H; B10-B01B; B14-A01; B14-A02; B14-A03; B14-A04; B14-C03; B14-C09; B14-F02B2; B14-F02D; B14-F02F2; B14-F03; B14-G02A; B14-G02C; B14-G02D; B14-H01; B14-J05B; B14-K01; B14-N03; B14-N06B; B14-N16; B14-N17; B14-P03; B14-S06

M1 *05* DCN: RAEG82-K; RAEG82-T; RAEG82-M

M1 *06* DCN: RA09LI-K; RA09LI-T; RA09LI-M; RA003V-K; RA003V-T; RA003V-M

M1 *07* DCN: RA0DNM-K; RA0DNM-T; RA0DNM-M; RA0KDA-K; RA0KDA-T; RA0KDA-M

M1 *08* DCN: RA02UP-K; RA02UP-T; RA02UP-M

M1 *09* DCN: R06364-K; R06364-T; R06364-M; R16207-K; R16207-T; R16207-M

M1 *10* DCN: RA022K-K; RA022K-T; RA022K-M

M2 *01* DCN: RA4TIW-K; RA4TIW-T; RA4TIW-M; RA4TIW-U

M2 *02* DCN: RACI5Z-K; RACI5Z-T; RACI5Z-M; RACI5Z-U

M2 *03* DCN: 0132-51801-K; 0132-51801-T; 0132-51801-M; 0132-51801-U

M2 *04* DCN: 0132-51802-K; 0132-51802-T; 0132-51802-M; 0132-51802-U

M2 *11* DCN: R01166-K; R01166-T; R01166-M

M2 *12* DCN: RA035F-K; RA035F-T; RA035F-M; RA2PVY-K; RA2PVY-T; RA2PVY-M

M2 *13* DCN: R10440-K; R10440-T; R10440-M

M2 *14* DCN: RA01E9-K; RA01E9-T; RA01E9-M

M2 *15* DCN: RA035H-K; RA035H-T; RA035H-M

M2 *16* DCN: R10124-K; R10124-T; R10124-M

M2 *17* DCN: R02028-K; R02028-T; R02028-M; R08024-K; R08024-T; R08024-M

M2 *18* DCN: R00125-K; R00125-T; R00125-M; R17770-K; R17770-T; R17770-M

M2 *19* DCN: R08225-K; R08225-T; R08225-M

M2 *20* DCN: RA021Q-K; RA021Q-T; RA021Q-M

M2 *21* DCN: R17804-K; R17804-T; R17804-M

M2 *22* DCN: R07202-K; R07202-T; R07202-M

M5 *23* DCN: R00002-K; R00002-T; R00002-M; R14648-K; R14648-T; R14648-M

DCRE 433262-0-0-0; 817201-0-0-0; 869582-0-0-0; 91489-0-0-0; 114126-0-0-0; 94444-0-0-0; 97946-0-0-0; 97854-0-0-0; 106545-2-0-0; 109181-1-0-0; 14620-0-0-0; 93613-1-0-0; 98147-1-0-0; 91082-0-0-0; 8769-1-0-0; 110156-1-0-0; 92243-0-0-0; 8220-2-0-0; 133806-1-0-0; 10897-0-0-0; 88752-2-0-0

ABEX

UPTX: 20040621

SPECIFIC COMPOUNDS - The use of 3-(3,4-dimethoxy-phenyl)-3-(1-oxo-1,3-dihydro-isoindol-2-yl)-propionamide and cyclopropanecarboxylic acid (2-(1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl)-3-oxo-2,3-dihydro-1H-isoindol-4-yl)-amide is specifically claimed as (I).

ADMINISTRATION - Administration of (I) is 1-10000 mg/day (claimed), orally, mucosally, parenterally, topically, transdermally or transcutaneously.

TECH

UPTX: 20040621

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: The treatment of cancer further comprises administration of a second active ingredient, radiation therapy, hormonal therapy, biological therapy or immunotherapy. The disease associated with undesired angiogenesis further comprises administering a second active ingredient (IV). (IV) is hematopoietic growth factor, cytokine, anti-cancer agent, antibiotic, cyclooxygenase (COX)-2 inhibitor, immunomodulatory agent, immunosuppressive agent, corticosteroid or a pharmacologically active mutant or derivative or a combination (preferably oblimersen, melphalan, granulocyte-colony stimulating factor (G-CSF), granulocyte macrophage (GM)-CSF, EPO (preferably Epogen (RTM; epoetin alpha)), topotecan, pentoxifylline, taxotere, irinotecan, COX-2 inhibitor, ciprofloxacin, dexamethasone, doxorubicin, vincristine, interleukin (IL)-2, interferon (IFN), dacarbazine, Ara-C, vinorelbine, isotretinoin or a salt, solvate or stereoisomer or a pharmacologically active mutant or derivative or a

combination). (I) is an azetidine derivative of formula (II) or pyrrol-2-one derivative of formula (III). (I) is administered before, during or after surgery directed at relieving, reducing or avoiding a symptom of a specific cancer in the patient. (IV) is administered prior to, during or after transplanting umbilical cord blood, placental blood, peripheral blood stem cell, hematopoietic stem cell preparation or bone marrow in the patient. (I) is administered prior to, during or after the administration of (IV), radiation therapy, hormonal therapy, biological therapy or immunotherapy. (I), (II) and (III) are enantiomerically pure.
 n = 1-3;
 R5 = o-phenylene (optionally substituted with 1-4 substituents of T);
 T = nitro, CN, CF₃, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxo, carboxy, OH, amino, alkylamino, dialkylamino, acylamino, 1-10C alkyl or halo;
 R7 = phenyl (optionally substituted with one or more of Ta), benzyl (optionally substituted with 1-3 of Ta), naphthyl or benzyloxy;
 Ta = nitro, CN, CF₃, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxo, carboxy, OH, amino, 1-10C alkyl, 1-10C alkoxy or halo;
 R12 = OH, 1-12C alkoxy or -N(R8R9);
 R8 = H or 1-10C alkyl;
 R9 = R8, COR10 or SO₂R10; and
 R10 = R8 or phenyl;
 R1, R2 = H or lower alkyl; or
 CR1R2 = o-phenylene, o-naphthylene, or cyclohexene-1,2-diyl (optionally substituted with 1-4 substituents of T');
 T' = nitro, CN, CF₃, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxo, carboxy, OH, amino, alkylamino, dialkylamino, acylamino, 1-10C alkyl, 1-10C alkoxy or halo);
 R3 = phenyl substituted with 1-4 substituents of T, 1-10C alkylthio, benzyloxy, 3-6C cycloalkoxy, 4-6C-cycloalkylidenemethyl, 3-10C -alkylidenemethyl or indanyloxy;
 R4 = H, 1-6C alkyl, phenyl or benzyl;
 R4' = H or 1-6C alkyl;
 R5' = CH₂, CH₂-CO, SO₂, S or NHCO; and
 n' = 0-2.

L42 ANSWER 3 OF 5 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN

AN 2004-388904 [36] WPIX

DNC C2004-145546

TI Use of selective cytokine inhibitory drugs, for treating, preventing or managing macular degeneration, e.g. wet or dry macular degeneration, age-related maculopathy, Best's disease, fundus flavimaculatus, or vitelliform.

DC B04 B05 D16

IN ZELDIS, J B

PA (ZELD-I) ZELDIS J B; (CELG-N) CELGENE CORP

CYC 110

PI US--2004091454 A1 20040513 (200436)* 19 A61K-038-21

WO--2004041181 A2 20040521 (200436) EN A61K-000-00

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE

LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK

DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP

KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG

PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ

VC VN YU ZA ZM ZW

AU--2003285107 A1 20040607 (200469) A61K-038-21

WO--2005044269 A1 20050519 (200534) EN A61K-031-445

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE

LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE

DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG

KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ

OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG

US UZ VC VN YU ZA ZM ZW

EP-----1567148 A2 20050831 (200561) EN A61K-031-40

R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV
MC MK NL PT RO SE SI SK TR

BR---200315889 A 20051004 (200566) A61K-031-40
TW---200418455 A 20041001 (200608) A61K-031-4035
JP---2006509743 W 20060323 (200623) 36 A61K-045-00
KR--2005062649 A 20050623 (200641) A61K-031-404
CN-----1731997 A 20060208 (200643) A61K-031-40

ADT US--2004091454 A1 Provisional 2002US-422900P 20021031, 2003US-0699110
20031030; WO--2004041181 A2 2003WO-US34535 20031031; AU--2003285107 A1
2003AU-0285107 20031031; WO--2005044269 A1 2004WO-US13253 20040428;
EP-----1567148 A2 2003EP-0779423 20031031, 2003WO-US34535 20031031;
BR---200315889 A 2003BR-0015889 20031031, 2003WO-US34535 20031031;
TW---200418455 A 2003TW-0130486 20031031; JP--2006509743 W 2003WO-US34535
20031031, 2004JP-0550274 20031031; KR--2005062649 A 2003WO-US34535
20031031, 2005KR-0707608 20050429; CN-----1731997 A 2003CN-80108090
20031031

FDT AU--2003285107 A1 Based on WO--2004041181; EP-----1567148 A2 Based on
WO--2004041181; BR---200315889 A Based on WO--2004041181; JP--2006509743 W
Based on WO--2004041181; KR--2005062649 A Based on WO--2004041181

PRAI 2002US-422900P 20021031; 2003US-0699110 20031030

IC ICM A61K-000-00; A61K-031-40; A61K-031-4035; A61K-031-404; A61K-031-445;
A61K-038-21; A61K-045-00
ICS A61K-031-00; A61K-031-403; A61K-031-409; A61K-031-4523; A61K-031-454;
A61K-031-522; A61K-031-545; A61K-031-557; A61K-031-56; A61K-039-395;
A61K-045-06; A61P-009-00; A61P-009-10;
A61P-027-00; A61P-027-02

AB US2004091454 A UPAB: 20040608

NOVELTY - A method of treating, preventing or managing macular
degeneration comprises administering to a patient a selective cytokine
inhibitory drug, or its pharmaceutical salt, solvate, or stereoisomer.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a
pharmaceutical composition comprising a selective cytokine inhibitory
drug, or its pharmaceutical salt, solvate, or stereoisomer, and a second
active agent capable of reducing or avoiding a symptom of macular
degeneration.

ACTIVITY - Ophthalmological.

No biological data given.

MECHANISM OF ACTION - Cytokine inhibitor.

USE - The method is useful for treating, preventing or managing
macular degeneration, such as wet macular degeneration, dry macular
degeneration, age-related macular degeneration, age-related maculopathy,
choroidal neovascularization, retinal pigment epithelium detachment,
atrophy of retinal pigment epithelium, Best's disease, vitelliform,
Stargardt's disease, juvenile macular dystrophy, fundus flavimaculatus,
Behr's disease, Sorsby's disease, Doyne's disease, honeycomb dystrophy, or
macular damaging condition (claimed).

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B04-A06; B04-G02; B04-H03; B04-H05; B04-H21; B04-J02; B04-J05;
B05-A02; B06-H; B07-H; B14-F02F2; B14-L05; B14-N03; D05-H11

M1 *08* DCN: RA1PSH-K; RA1PSH-M

M1 *09* DCN: RA022K-K; RA022K-M

M1 *10* DCN: RA078O-K; RA078O-M

M1 *11* DCN: RA00F4-K; RA00F4-M

M1 *12* DCN: RA0WK5-K; RA0WK5-M

M1 *13* DCN: RA0WK5-K; RA0WK5-M

M2 *01* DCN: RA4TIW-K; RA4TIW-T; RA4TIW-M; RA4TIW-U

M2 *02* DCN: RAE95F-K; RAE95F-T; RAE95F-M; RAE95F-U

M2 *03* DCN: RAE95E-K; RAE95E-T; RAE95E-M; RAE95E-U

M2 *04* DCN: RACI5Z-K; RACI5Z-T; RACI5Z-M;

RACI5Z-U

M2 *05* DCN: 0131-62201-K; 0131-62201-T; 0131-62201-M; 0131-62201-U

M2 *06* DCN: 0131-62202-K; 0131-62202-T; 0131-62202-M; 0131-62202-U

M2 *07* DCN: 0131-62203-K; 0131-62203-T; 0131-62203-M; 0131-62203-U

M2 *14* DCN: R23692-K; R23692-T; R23692-M

M2 *15* DCN: RA1Q SX-K; RA1Q SX-M

M2 *16* DCN: R10440-K; R10440-M

M2 *17* DCN: RA1ZZX-K; RA1ZZX-M

DCRE 433262-0-0-0; 433262-2-0-0; 433262-1-0-0; 817201-0-0-0; 282324-0-0-0;
97854-0-0-0; 107425-0-0-0; 107436-0-0-0; 97861-0-0-0; 108692-0-0-0;
88666-1-0-0; 14620-0-0-0; 94674-0-0-0; 97861-0-0-0

ABEX UPTX: 20040608

WIDER DISCLOSURE - Also disclosed is a kit comprising the pharmaceutical composition, and additional active agents.

ADMINISTRATION - The selective cytokine inhibitory drug is administered at a dose of 1-10000 mg. Administration can be parenteral (e.g. intravitreal, intravenous, intramuscular, or intraarterial), oral, topical or mucosal.

TECH UPTX: 20040608

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The method further comprises administering a second active agent selected from a steroid, a light sensitizer, an integrin, an antioxidant, an interferon, a xanthine derivative, a growth hormone, a neutrotrophic factor, a regulator of neovascularization, an anti-vascular endothelial growth factor (VEGF) antibody, a prostaglandin, an antibiotic, a phytoestrogen, an anti-inflammatory compound, an antiangiogenesis compound (such as thalidomide), thalidomide, verteporfin, purlytin, an angiostatic steroid, rhuFab, interferon-2alpha, pentoxifylline, or its pharmaceutical salt, solvate, or stereoisomer.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Drug: The selective cytokine inhibitory drug is stereomerically pure. Specifically, the method comprises administering 3-(3,4-dimethoxy-phenyl)-3-(1-oxo-1,3-dihydro-isoindol-2-yl)-propionamide, cyclopropanecarboxylic acid (2-(1(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl)-3-oxo-2,3-dihydro-1H-isoindol-4-yl)-amide, or their pharmaceutical salt, solvate, or stereoisomer, where the compounds are enantiomerically pure. The selective cytokine inhibitory drug is formula (I), (II) or (III).

For (I),

n = 1-3;

R5 = o-phenylene, unsubstituted or substituted with 1-4 substituents each selected independently from nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxo, carboxy, hydroxy, amino, alkylamino, dialkylamino, acylamino, 1-10C alkyl, 1-10C, and halo;

R7 = phenyl or phenyl substituted with one or more substituents each selected independently from nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxo, carboxy, hydroxy, amino, alkyl of 1-10 carbon atoms, alkoxy of 1-10 carbon atoms, and halo; benzyl unsubstituted or substituted with 1-3 substituents selected from nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxo, carboxy, hydroxy, amino, 1-10C alkyl, 1-10C alkoxy and halo; naphthyl, or benzyloxy;

R12 = -OH, 1-12C alkoxy, or (Ia);

R8 = hydrogen or 1-10C alkyl;

R9 = hydrogen, 1-10C alkyl, -COR10, or -SO2R10; and

R10 = hydrogen, 1-10C alkyl, or phenyl

For (II),

R1 and R2 = when taken independently of each other, is hydrogen, lower alkyl, or R1 and R2, when taken together with the depicted carbon atoms to which each is bound, is o-phenylene, o-naphthylene, or cyclohexene-1,2-diyl, unsubstituted or substituted with 1-4 substituents each selected independently from nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxo, carboxy, hydroxy, amino, alkylamino, dialkylamino, acylamino, 1-10C alkyl, 1-10C alkoxy, and halo;

R3 = phenyl substituted with from 1-4 substituents selected from nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxo, carboxy, hydroxy, amino, 1-10C alkyl, 1-10C alkoxy, 1-10C alkylthio, benzyloxy, 3-6C cycloalkoxy, 4-6C cycloalkylidenemethyl, 3-10C alkylidenemethyl, indanyloxy, and halo;

R4 = hydrogen, alkyl of 1-6 carbon atoms, phenyl, or benzyl;

R4' = H or 1-6C alkyl

R5 = -CH₂-, -CH₂-CO-, -SO₂-, -S-, or -NHCO-; and

n = 0, 1, or 2

For (II),

Y = C=O, CH₂, SO₂, or CH₂C=O;

R1, R2, R3, and R4 = independently selected from hydrogen, halo, 1-2C, 1-4C alkoxy, nitro, cyano, hydroxy, or -NR₈R₉; or any 2 of R1, R2, R3, and R4 on adjacent carbon atoms, together with the depicted phenylene ring are naphthylidene;

R5 and R6 = independently of the other, is hydrogen, 1-4C alkyl, 1-4C alkoxy, cyano, or cycloalkoxy of up to 18 carbon atoms;

R7 = hydroxy, alkyl of 1-8 carbon atoms, phenyl, benzyl, or NR₈R₉;

R8 and R9 = taken independently of the other is hydrogen, 1-8C alkyl,

phenyl, or benzyl; R8 or R9 is hydrogen and the other is -COR₁₀ or -SO₂R₁₀; or R8 and R9 taken together are tetramethylene, pentamethylene,

hexamethylene, or -CH₂CH₂X₁CH₂CH₂- in which X₁ is -O-, -S-, or -NH-; and

R8' and R9' = taken independently of the other is hydrogen, alkyl of 1-8 carbon atoms, phenyl, or benzyl; R8' or R9' = hydrogen and the other is -CO₁₀'- or -SO₂R₁₀'; or R8' and R9' = taken together are tetramethylene, pentamethylene, hexamethylene, or -CH₂CH₂X₂CH₂CH₂- in which X₂ -O-, -S-, or -NH-.

The selective cytokine inhibitory drug, or its salt, solvate, or stereoisomer may be administered before, during or after surgical intervention directed at reducing or avoiding a symptom of macular degeneration in the patient. The surgical intervention may be light therapy, laser therapy, radiation therapy, retinal pigment epithelium transplantation, or foveal translocation.

L42 ANSWER 4 OF 5 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN

AN 2004-365426 [34] WPIX

DNC C2004-137967

TI Use of a selective cytokine inhibitory drug in the treatment, prevention, modification or management of pain e.g. visceral pain, migraine, tension type headache or post-operative pain.

DC B05

IN FALECK, H; MANNING, D C; ZELDIS, J B

PA (FALE-I) FALECK H; (MANN-I) MANNING D C; (ZELD-I) ZELDIS J B; (CELG-N) CELGENE CORP

CYC 108

PI WO--2004037207 A2 20040506 (200434)* EN 62 A61K-000-00

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS

LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK

DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP

KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG

PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ

VC VN YU ZA ZM ZW

US--2004087558 A1 20040506 (200434) A61K-031-60

AU--2003284979 A1 20040513 (200468) A61K-000-00

EP-----1562586 A2 20050817 (200554) EN A61K-031-405

R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV

MC MK NL PT RO SE SI SK TR

BR---200315593 A 20050906 (200560) A61K-031-405

TW---200412943 A 20040801 (200581) A61K-031-395

JP--2006505591 W 20060216 (200614) 48 A61K-045-00

CN-----1731998 A 20060208 (200643) A61K-031-403

KR--2005072113 A 20050708 (200643) A61K-031-405

ADT WO--2004037207 A2 2003WO-US034005 20031024; US--2004087558 A1 Provisional

2002US-421004P 20021024, 2003US-0693722 20031023; AU--2003284979 A1

2003AU-0284979 20031024; EP-----1562586 A2 2003EP-0779299 20031024,

2003WO-US34005 20031024; BR---200315593 A 2003BR-0015593 20031024,

2003WO-US34005 20031024; TW---200412943 A 2003TW-0129607 20031024;

JP--2006505591 W 2003WO-US34005 20031024, 2004JP-0547196 20031024;

CN-----1731998 A 2003CN-80107547 20031024; KR--2005072113 A 2003WO-US34005

20031024, 2005KR-0707018 20050422

FDT AU--2003284979 A1 Based on WO--2004037207; EP-----1562586 A2 Based on

WO--2004037207; BR---200315593 A Based on WO--2004037207; JP--2006505591 W

Based on WO--2004037207; KR--2005072113 A Based on WO--2004037207

PRAI 2002US-421004P 20021024; 2003US-0693722 20031023

IC ICM A61K-000-00; A61K-031-395; A61K-031-403; A61K-031-405; A61K-031-60;
A61K-045-00

ICS A61K-031-095; A61K-031-10; A61K-031-19; A61K-031-192; A61K-031-40;
A61K-031-445; A61K-031-485; A61K-031-573; A61P-025-00; A61P-025-04;
A61P-025-06; A61P-029-00; A61P-043-00

AB WO2004037207 A UPAB: 20040527

NOVELTY - Treatment, prevention, modification or management of pain comprises administration of a selective cytokine inhibitory drug (I) or its salt, solvate or stereoisomer.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a composition comprising (I) or its salt, solvate or stereoisomer and (II), capable of relieving or reducing pain.

ACTIVITY - Analgesic; Antimigraine.

MECHANISM OF ACTION - Selective cytokine inhibitor.

USE - (I) is useful in the treatment, prevention, modification or management of pain (nociceptive pain and/or neuropathic pain, visceral pain, migraine, tension type headache or post-operative pain) associated with chemical/thermal burn, cut of the skin, contusion of the skin, osteoarthritis, rheumatoid arthritis, tendonitis or myofascial pain (particularly diabetic neuropathy, post herpetic neuralgia, trigeminal neuralgia, post-stroke pain, complex regional pain syndrome (type I or II), sympathetic maintained pain syndrome, reflex sympathetic dystrophy, reflex neurovascular dystrophy, reflex dystrophy, spinal cord injury pain, Sudeck atrophy of bone, algoneurodystrophy, shoulder hand syndrome, post-traumatic dystrophy, cancer related pain, phantom limb pain, fibromyalgia, chronic fatigue syndrome, radiculopathy, luetic neuropathy or painful neuropathic condition induced from a drug (iatrogenically induced by vincristine, velcade or thalidomide)) (claimed).

The biological effectiveness of compounds (I) (3-(3,4-dimethoxy-phenyl)-3-(1-oxo-1,3-dihydro-isoindol-2-yl)-propionamide) were tested in patients with pain syndromes for three to six months. The results showed that (I) have analgesic benefit in this disease.

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B01-B01; B04-A04; B06-A01; B06-A03; B06-D01; B06-D03; B06-D09;
B06-D12; B06-E05; B07-D04D; B07-D05; B07-D08; B07-D09; B10-B02E;
B10-B04B; B10-C03; B10-C04C; B10-C04E; B10-D03; B14-A01; B14-A04;
B14-C01; B14-C03; B14-C07; B14-D05C; B14-F01; B14-F02B; B14-G02;
B14-G03; B14-J01A1; B14-J01B4; B14-J02C1; B14-J02D1; B14-J05A;
B14-J07; B14-L06

M2 *01* DCN: RA4TIW-K; RA4TIW-T; RA4TIW-M; RA4TIW-U

M2 *02* DCN: RACI5Z-K; RACI5Z-T; RACI5Z-M;
RACI5Z-U

M2 *03* DCN: 0130-78501-K; 0130-78501-T; 0130-78501-M; 0130-78501-U

M2 *04* DCN: 0130-78502-K; 0130-78502-T; 0130-78502-M; 0130-78502-U

M2 *05* DCN: 0130-78503-K; 0130-78503-T; 0130-78503-M; 0130-78503-U

M2 *06* DCN: 0130-78504-K; 0130-78504-T; 0130-78504-M; 0130-78504-U

M2 *07* DCN: 0130-78505-K; 0130-78505-T; 0130-78505-M; 0130-78505-U

M2 *08* DCN: R00034-K; R00034-T; R00034-M; R06663-K; R06663-T; R06663-M

M2 *09* DCN: RA027G-K; RA027G-T; RA027G-M

M2 *10* DCN: R01651-K; R01651-T; R01651-M

M2 *11* DCN: R18780-K; R18780-T; R18780-M

M2 *12* DCN: R01203-K; R01203-T; R01203-M

M2 *13* DCN: R21564-K; R21564-T; R21564-M

M2 *14* DCN: R00129-K; R00129-T; R00129-M; R04339-K; R04339-T; R04339-M

M2 *15* DCN: R03911-K; R03911-T; R03911-M

M2 *16* DCN: R03027-K; R03027-T; R03027-M; R11668-K; R11668-T; R11668-M

M2 *17* DCN: R01627-K; R01627-T; R01627-M; R06674-K; R06674-T; R06674-M

M2 *18* DCN: R06854-K; R06854-T; R06854-M; R16303-K; R16303-T; R16303-M

M2 *19* DCN: R00130-K; R00130-T; R00130-M; R16302-K; R16302-T; R16302-M

M2 *20* DCN: R07434-K; R07434-T; R07434-M

M2 *21* DCN: R03169-K; R03169-T; R03169-M; R10726-K; R10726-T; R10726-M

M2 *22* DCN: R01254-K; R01254-T; R01254-M; R16301-K; R16301-T; R16301-M

M2 *23* DCN: R00758-K; R00758-T; R00758-M; R16282-K; R16282-T; R16282-M
 M2 *24* DCN: R01987-K; R01987-T; R01987-M; R06547-K; R06547-T; R06547-M;
 R11757-K; R11757-T; R11757-M; R14131-K; R14131-T; R14131-M
 M2 *25* DCN: RA01BE-K; RA01BE-T; RA01BE-M
 M2 *26* DCN: R01073-K; R01073-T; R01073-M
 M2 *27* DCN: R00022-K; R00022-T; R00022-M; R16160-K; R16160-T; R16160-M
 M2 *28* DCN: R00023-K; R00023-T; R00023-M; R11478-K; R11478-T; R11478-M
 M2 *29* DCN: R07411-K; R07411-T; R07411-M; R16161-K; R16161-T; R16161-M
 M5 *30* DCN: R00067-K; R00067-T; R00067-M

DCRE 433262-0-0-0; 817201-0-0-0; 87874-0-0-0; 127393-0-0-0; 61643-0-0-0;
 95795-0-0-0; 44063-0-0-0; 102950-0-0-0; 77147-0-0-0; 110010-0-4-0;
 6754-0-0-0; 91319-0-0-0; 103043-1-0-0; 13312-0-0-0; 148654-1-0-0;
 97160-1-0-0; 95048-0-0-0; 5735-0-0-0; 7556-0-0-0; 72366-0-1-0;
 35431-1-0-0; 87308-0-0-0; 97730-0-0-0; 93683-0-0-0; 104629-1-0-0

ABEX UPTX: 20040527

SPECIFIC COMPOUNDS - The use of salicylic acid acetate, celecoxib, ketamine, gabapentin, carbamazepine, oxcarbazepine, phenytoin, sodium valproate, prednisone, nifedipine, clonidine, oxycodone, meperidine, morphine sulfate, hydromorphone, fentanyl, acetaminophen, ibuprofen, naproxen sodium, griseofulvin, amitriptyline, imipramine and doxepin is specifically claimed as (II). The use of 3-(3,4-dimethoxy-phenyl)-3-(1-oxo-1,3-dihydro-isoindol-2-yl)-propionamide and cyclopropanecarboxylic acid (2-(1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl)-3-oxo-2,3-dihydro-1H-isoindol-4-yl) -amide is specifically claimed as (I).

ADMINISTRATION - Administration of (I) is 1-10,000 (preferably 100-800) mg/day, orally. Administration of (II) is 1-3,500 (preferably 25-250) mg/day, orally, intravenously, intramuscularly, subcutaneously, mucosally, or transdermally.

TECH UPTX: 20040527

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Process: The method further comprises the administration of at least one second active agent (II) that is capable of relieving or reducing pain. (I) is administered before, during or after surgery, psychological or physical therapy directed at reducing or avoiding a symptom of pain in the patient.

Preferred Components: (II) is an antidepressant, antihypertensive agent, anxiolytic agent, calcium channel blocker, alpha-adrenergic receptor agonist, alpha-adrenergic receptor antagonist, ketamine, anesthetic, muscle relaxant, non-narcotic analgesic, opioid analgesic, anti-inflammatory agent, immunomodulatory agent, immunosuppressive agent, corticosteroid, anticonvulsant, cyclooxygenase-2 inhibitor and/or hyperbaric oxygen. The stereoisomers of (I) are enantiomerically pure. (I) is preferably a carbonyl compound of formulae (1), (2) or (3).

R5 = o-phenylene (optionally substituted with 1-4 of (di)alkylamino, acylamino or T);

R7 = phenyl (optionally substituted with T), benzyl (optionally substituted with 1-3 of T), naphthyl or benzyloxy;

R12 = OH, 1-12C alkoxy or N(R8)R9;

R8 = H or 1-10C alkyl; and

R9 = H, 1-10C alkyl, COR10 or SO2R10;

R10 = H, 1-10C alkyl or phenyl;

T = NO2, CN, CF3, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, COOH, OH, NH2, 1-10C alkyl, 1-10C alkoxy or halo; and n = 1-3.

Either R1, R2 = H or lower alkyl; or

CR1R2 = o-phenylene, o-naphthylene or cyclohexene-1,2-diyl (optionally substituted with 1-4 of (di)alkylamino, acylamino or T);

R3 = phenyl (substituted with 1-4 of NO2, CN, CF3, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, COOH, OH, NH2, 1-10C alkyl, 1-10C alkoxy, 1-10C alkylthio, benzyloxy, 3-6C cycloalkoxy, 4-6C cycloalkylidenemethyl, 3-10C alkylidenemethyl, indanyloxy or halo);

R4 = H, 1-6C alkyl, phenyl or benzyl;

R4 = H or 1-6C alkyl;

R5 = CH2, CH2-CO, SO2, S or NHCO; and

n = 0-2.

Y' = C-O, CH2, SO2 or CH2C-O;

asterisk = center of chirality;
 R1-R4 = H, halo, 1-4C alkyl, 1-4C alkoxy, NO₂, CN, OH or NR₈R₉; or
 any two of R1, R2, R3 or R4 (on adjacent carbon atoms together with
 phenylene) = naphthylidene;
 R5, R6 = H, 1-4C alkyl, 1-4C alkoxy, CN or 1-18C cycloalkoxy;
 R7 = OH, 1-8 alkyl, phenyl, benzyl or NR₈ R₉;
 either R8, R9 = H, 1-8C alkyl, phenyl or benzyl; or
 R8R9 = tetramethylene, pentamethylene, hexamethylene or CH₂CH₂X₁CH₂CH₂; or
 either R8 = H; and
 R9 = COR₁₀ or SO₂R₁₀; or vice versa;
 X₁ = O, S or NH;
 either R8', R9' = H, 1-8C alkyl, phenyl or benzyl; or
 R8'R9' = tetramethylene, pentamethylene, hexamethylene or CH₂CH₂X₂CH₂CH₂;
 or
 either R8' = H; and
 R9' = COR₁₀' or SO₂R₁₀'; or vice versa; and
 X₂ = O, S or NH.

L42 ANSWER 5 OF 5 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
 AN 2004-034763 [03] WPIX
 CR 2004-034766 [03]; 2004-420073 [39]; 2004-420074 [39]; 2005-031046 [03]
 DNC C2004-011468
 TI Use of selective cytokine inhibitory drug e.g. 3-(3,4-dimethoxy-phenyl)-3-(1-oxo-1,3-dihydro-isoindol-2-yl)-propionamide to treat cancers and diseases associated with undesired angiogenesis.
 DC B03
 IN ZELDIS, J B
 PA (CELG-N) CELGENE CORP; (BARE-I) BARER S J
 CYC 109
 PI WO--2003097040 A1 20031127 (200403)* EN 62 A61K-031-40
 RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS
 LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
 DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
 KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
 RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA
 ZM ZW
 AU--2003234624 A1 20031202 (200442) A61K-031-40
 KR--2005010812 A 20050128 (200535) A61K-031-445
 EP-----1556033 A1 20050727 (200549) EN A61K-031-40
 R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV
 MC MK NL PT RO SE SI SK TR
 JP--2005530780 W 20051013 (200568) 49 A61K-045-00
 MX--2004011310 A1 20050301 (200568) A61K-031-40
 US--2005234017 A1 20051020 (200569) A61K-031-724
 WO--2005112918 A1 20051201 (200580)# EN A61K-031-40
 RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE
 LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE
 DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG
 KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ
 OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG
 US UZ VC VN YU ZA ZM ZW
 CN-----1668296 A 20050914 (200607) A61K-031-40
 CN-----1697655 A 20051116 (200620) A61K-031-445
 CN-----1735412 A 20060215 (200643) A61K-031-44
 ADT WO--2003097040 A1 2003WO-US015468 20030516; AU--2003234624 A1
 2003AU-0234624 20030516; KR--2005010812 A 2004KR-0718550 20041117;
 EP-----1556033 A1 2003EP-0728967 20030516, 2003WO-US15468 20030516;
 JP--2005530780 W 2003WO-US15468 20030516, 2004JP-0505039 20030516;
 MX--2004011310 A1 2003WO-US15468 20030516, 2004MX-0011310 20041115;
 US--2005234017 A1 2003WO-US15468 20030516, 2005US-0515270 20050523;
 WO--2005112918 A1 2004WO-US14002 20040505; CN-----1668296 A 2003CN-0816968
 20030516; CN-----1697655 A 2003CN-0816899 20030516; CN-----1735412 A
 2003CN-80108390 20031106
 FDT AU--2003234624 A1 Based on WO--2003097040; EP-----1556033 A1 Based on

WO--2003097040; JP--2005530780 W Based on WO--2003097040; MX--2004011310
A1 Based on WO--2003097040

PRAI 2002US-424601P 20021106; 2002US-380842P 20020517;
2004WO-US014002 20040505; 2002US-424600P 20021106
IC ICM A61K-031-40; A61K-031-44; A61K-031-445; A61K-031-724; A61K-045-00
ICS A61K-031-198; A61K-031-4035; A61K-031-415; A61K-031-425;
A61K-031-496; A61K-031-515; A61K-031-573; A61K-031-704; A61K-038-18;
A61K-038-20; A61K-045-06; A61P-001-04; A61P-001-16; A61P-003-06;
A61P-007-02; A61P-007-06; A61P-009-04; A61P-009-10
; A61P-009-14; A61P-011-00; A61P-011-06; A61P-011-16;
A61P-017-02; A61P-017-06; A61P-017-10; A61P-019-02; A61P-019-08;
A61P-025-00; A61P-027-02; A61P-027-06; A61P-027-10; A61P-027-14;
A61P-029-00; A61P-031-00; A61P-031-04; A61P-031-10; A61P-031-12;
A61P-031-18; A61P-033-00; A61P-033-02; A61P-033-06; A61P-035-00;
A61P-035-02; A61P-035-04; A61P-037-00; A61P-037-06; A61P-037-08;
A61P-041-00; A61P-043-00; C07D-401-00

AB WO2003097040 A UPAB: 20060706

NOVELTY - Treating, managing or preventing a specific cancer or disease associated with undesired angiogenesis comprises selective cytokine inhibitory drug and their salts, solvates, hydrates, stereoisomers, clathrates or prodrugs.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) composition comprising a selective cytokine inhibitory drug and their salts, solvates, hydrates, stereoisomers, clathrates or prodrugs and a second active ingredient (A); and

(2) a kit comprising a selective cytokine inhibitor drug and second active ingredient (chosen from hematopoietic growth factor, cytokine, anticancer agents, antibiotic, a cyclooxygenase-2 inhibitor, immunomodulatory agent, immunosuppressive agent, corticosteroid or their mutants and/or derivatives) or umbilical cord blood, placental blood, peripheral blood stem cell, hematopoietic stem cell preparation or bone marrow.

ACTIVITY - Cytostatic; Antiangiogenic; Antidiabetic; Ophthalmological; Immunosuppressive; Anti-HIV; Antiseborrheic; Dermatological; Antibacterial; Antiulcer; Virucide; Auditory; Protozoacide; Antiarthritic; Antirheumatic; Antiinflammatory; Vulnerary; Antianemic.

Selective cytokine inhibitory drug was tested in patients with relapsed and refractory Dune-salmon stage III multiple myeloma. The results showed that the therapy comprising selective cytokine inhibitory drug in combination with melphalan and dexamethasone was highly active and generally tolerated in heavily pretreated multiple myeloma patients whose prognosis was otherwise poor.

MECHANISM OF ACTION - Cytokine production inhibitor; Tumor necrosis factor-alpha inhibitor.

USE - The selective cytokine inhibitory drug is useful in the treatment of specific cancer (preferably advanced malignancy, amyloidosis, locally advanced bladder cancer, metastatic transitional cell bladder cancer, relapsed brain tumor, progressive brain tumor, neuroblastoma, meningioma, hemangiopericytoma, multiple brain metastase, glioblastoma multiforms, glioblastoma, brain stem glioma, poor prognosis malignant brain tumor, malignant glioma, anaplastic astrocytoma, anaplastic oligodendroglioma, metastatic breast cancer, neuroendocrine tumor, rectal adenocarcinoma, Dukes C and D colorectal cancer, unrespectable colorectal carcinoma, metastatic hepatocellular carcinoma, Kaposi's sarcoma, karotype acute myeloblastic leukemia, Hodgkin's lymphoma, non-Hodgkin's lymphoma, cutaneous T-cell lymphoma, cutaneous B-Cell lymphoma, diffuse large B-Cell lymphoma, low grade follicular lymphoma, malignant melanoma, malignant mesothelioma, stage IIIB non-small cell lung cancer, malignant pleural effusion mesothelioma syndrome, multiple myeloma, peritoneal carcinoma, papillary serous carcinoma, gynecologic sarcoma, soft tissue sarcoma, scleroderma, cutaneous vasculitis, Langerhans cell histiocytosis, leiomyosarcoma, fibrodysplasia ossificans progressive, hormone refractory prostate cancer, resected high-risk soft tissue sarcoma, unresectable hepatocellular carcinoma, Waldenstrom's macroglobulinemia, smoldering myeloma, indolent myeloma, fallopian tube cancer, androgen independent

prostate cancer, androgen dependent stage IV non-metastatic prostate cancer, hormone-insensitive prostate cancer, chemotherapy-insensitive prostate cancer, papillary thyroid carcinoma, follicular thyroid carcinoma, medullary thyroid carcinoma or leiomyoma) and disease associated with undesired angiogenesis (preferably diabetic retinopathy, retinopathy of prematurity, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, proliferative vitreoretinopathy, trachoma, myopia, optic pits, epidemic keratoconjunctivitis, atopic keratitis, superior limbic keratitis, pterygium keratitis sicca, Sjogren's, acne rosacea, phlyctenulosis, syphilis, lipid degeneration, bacterial ulcer, fungal ulcer, Herpes simplex infection, Herpes zoster infection, protozoan infection, Kaposi's sarcoma, Mooren ulcer, Terrine's marginal degeneration, marginal keratolysis, rheumatoid arthritis, systemic lupus, polyarteritis, trauma, Wegener's sarcoidosis, scleritis, Steven's Johnson disease, periphigoid radial keratotomy, sickle cell anemia, sarcoid, pseudoxanthoma elasticum, Paget's disease, vein occlusion, artery occlusion, carotid obstructive disease, chronic uveitis, chronic vitritis, Lyme's disease, Eales disease, Behcet's disease, retinitis, thyroiditis, presumed ocular histoplasmosis, Best's disease, Stargardt's disease, pars planitis, chronic retinal detachment, hyperviscosity syndromes, toxoplasmosis, sclerosing cholangitis or rubeosis. The immunomodulatory compound is also useful in the reducing or avoiding an adverse effect associated with the administration of second active ingredient, radiation therapy, hormonal therapy, biological therapy or immuno therapy (all claimed).

ADVANTAGE - The selective cytokine inhibitory drug is useful in the treatment of various type of cancer and diseases associated with angiogenesis as well as to reduce or avoid the adverse side effects caused by the treatments such as radiation therapy and biological therapy.

Dwg.0/0

FS

CPI

FA

AB; GI; DCN

MC

CPI: B01-B02; B02-D; B02-T; B04-B03A; B04-B04D; B04-B04E; B04-F01; B04-H02B; B04-H04A; B04-H04C; B04-H07; B06-D03; B06-H; B07-H; B10-B01A; B10-C04A; B14-A01; B14-A01A2; B14-A02A3; B14-A03; B14-A04; B14-C03; B14-C09B; B14-D05C; B14-E08; B14-F02D; B14-F02F1; B14-F03; B14-G02; B14-G02A; B14-G02D; B14-H01; B14-J01B4; B14-J05B; B14-N03; B14-N17; B14-N17B; B14-N17D; B14-S04

M1 *17* DCN: RA09LI-K; RA09LI-T; RA09LI-M; RA003V-K; RA003V-T; RA003V-M

M1 *18* DCN: RA0DNM-K; RA0DNM-T; RA0DNM-M; RA0KDA-K; RA0KDA-T; RA0KDA-M

M1 *19* DCN: RA1WOE-K; RA1WOE-T; RA1WOE-M

M1 *20* DCN: RA04TA-K; RA04TA-T; RA04TA-M

M2 *01* DCN: RA4TIW-K; RA4TIW-T; RA4TIW-M; RA4TIW-U

M2 *02* DCN: RACI5Z-K; RACI5Z-T; RACI5Z-M; RACI5Z-U

M2 *03* DCN: 0115-62601-K; 0115-62601-T; 0115-62601-M; 0115-62601-U

M2 *04* DCN: 0115-62602-K; 0115-62602-T; 0115-62602-M; 0115-62602-U

M2 *05* DCN: R01166-K; R01166-T; R01166-M

M2 *06* DCN: RA035F-K; RA035F-T; RA035F-M; RA2PVY-K; RA2PVY-T; RA2PVY-M

M2 *07* DCN: R10440-K; R10440-T; R10440-M

M2 *08* DCN: RA01E9-K; RA01E9-T; RA01E9-M

M2 *09* DCN: R10124-K; R10124-T; R10124-M

M2 *10* DCN: R02028-K; R02028-T; R02028-M; R08024-K; R08024-T; R08024-M

M2 *11* DCN: R00125-K; R00125-T; R00125-M; R17770-K; R17770-T; R17770-M

M2 *12* DCN: R08225-K; R08225-T; R08225-M

M2 *13* DCN: RA021Q-K; RA021Q-T; RA021Q-M

M2 *14* DCN: R17804-K; R17804-T; R17804-M

M2 *15* DCN: R07202-K; R07202-T; R07202-M

M5 *16* DCN: R00002-K; R00002-T; R00002-M; R14648-K; R14648-T; R14648-M

DCRE 433262-0-0-0; 817201-0-0-0; 106545-2-0-0; 109181-1-0-0; 14620-0-0-0; 93613-1-0-0; 91082-0-0-0; 8769-1-0-0; 110156-1-0-0; 92243-0-0-0; 8220-2-0-0; 133806-1-0-0; 10897-0-0-0; 88752-2-0-0; 91489-0-0-0; 114126-0-0-0; 94348-0-0-0; 97947-0-0-0

ABEX

UPTX: 20040112

SPECIFIC COMPOUNDS - The use of 3-(3,4-dimethoxy-phenyl)-3-(1-oxo-1,3-

dihydro-isoindol-2-yl)-propionamide and cyclopropanecarboxylic acid (2-(1-(3-ethoxy-4-methoxy-phenyl)-2-methane sulfonyl-ethyl)-3-oxo-2,3-dihydro-1H-isoindol-4-yl)-amide are specifically claimed as selective cytokine inhibitory drug.

ADMINISTRATION - 1-5000 mg of cytokine inhibitory drug is administered per day (claimed). The composition (I) is administered by oral, mucosal (e.g. nasal, sublingual, vaginal, buccal or rectal), parenteral (e.g. subcutaneous, intravenous, bolus injection, intramuscular or intraarterial), topical (e.g. eye drops or other ophthalmic preparations), transdermal or transcutaneous routes. The dosage amount of second active ingredient is 1-1000 mg (preferably 50-200 mg).

TECH

UPTX: 20040112

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: The cytokine inhibitory drug is a compound of formula (I) or (II).

In (I),

R5 = O-phenylene optionally substituted with T and M;

R7 = phenyl, benzyl (all optionally substituted with T or 1-10C alkoxy), benzyloxy or naphthyl;

R12 = OH, 1-12C alkoxy or N(R8R9);

R8 = H or 1-10C alkyl;

R9 = H, 1-10C alkyl, COR10 or SO2R10;

R10 = H, 1-10C alkyl or phenyl;

T = NO2, CN, CF3, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxo, carboxy, OH, NH2, 1-10C alkyl or halo;

M = alkylamino, dialkylamino or acylamino; and

n = 0-3.

In (II),

R1, R2 = H or lower alkyl;

R1R2 + depicted carbon = O-phenylene, O-naphthylene or cyclohexane-1,2-diyl (optionally substituted with 1-4 groups of 1-10C alkoxy, T or M);

R3 = phenyl (optionally substituted with 1-4 groups of 1-10C alkoxy, T, M, 1-10C alkylthio, benzyloxy, 3-10C cycloalkoxy, 4-6C cycloalkylidene methyl, 3-10C alkylidenemethyl or indanyloxy);

R4 = H, 1-6C alkyl, phenyl or benzyl;

R4a = H or 1-6C alkyl;

R5a = CH2, CH2CO, SO2, S or NHCO; and

n' = 0-2.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: The preferred compositions comprise the following:

(a) The treatment, management or prevention of a specific cancer (I) further comprises a second active ingredient, radiation therapy, hormonal therapy, biological therapy or immuno therapy;

(b) the treatment, management or prevention of a specific cancer further comprises a transplantation of umbilical cord blood, placental blood, peripheral blood stem cell, hematopoietic stem cell preparation or bone marrow in the patient (all are processed umbilical cord blood, processed placental blood, processed peripheral blood stem cell, processed hematopoietic stem cell preparation or processed bone marrow).

Preferred Process: In the treatment, management or prevention of a specific cancer, a selective cytokine inhibitor drug is administered prior to, after, during the administration of a second active ingredient, biological therapy, radiation therapy, hormonal therapy, immuno therapy (transplantation of cord blood, placental blood, peripheral blood stem cell, hematopoietic stem cell preparation or bone marrow in the patient) or surgery directed at relieving, reducing or avoiding a symptom of a specific cancer in the patient.

Preferred Components:

(a) The specific cancer is preferably refractory to conventional therapy;

(b) The selective cytokine inhibitory drug used is enantiomerically pure; and

(c) The second active ingredient is hematopoietic growth factor, cytokine, anti-cancer agent, antibiotic, Cox-2 inhibitor, immunomodulatory agent, immunosuppressive agent, corticosteroid or a pharmacologically active mutant or their derivative (preferably oblimersen, melphalan, G-CSF,

GM-CSF, EPO, a Cox-2 inhibitor, topotecan, pentoxifylline, ciprofloxacin, taxotere, iritotecan, dexamethasone, doxorubicin, vincristine, IL 2, IFN, dacarbazine, Ara-C, vinorelbine, isotretinoin or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate or their prodrug or a pharmacologically active mutant or derivative).

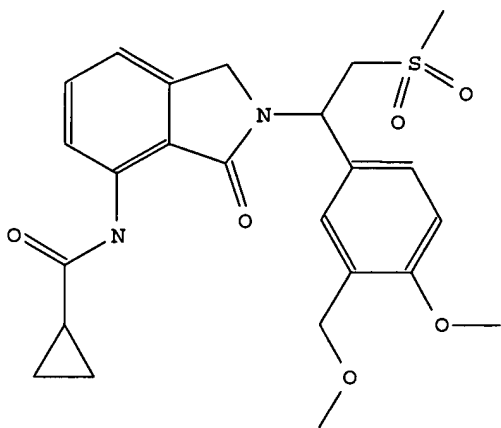
=> d ide l31 tot

L31 ANSWER 1 OF 4 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN

AN.S DCR-1178756

DCSE 1178756-0-0-0

CN.S Cyclopropanecarboxylic acid {2-[2-methanesulfonyl-1-(4-methoxy-3-methoxymethyl-phenyl)-ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide



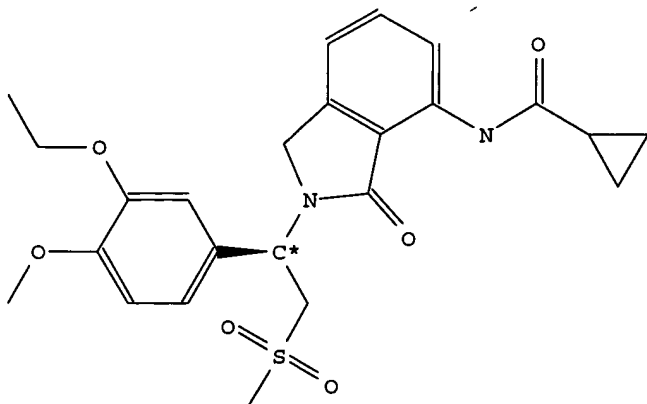
MF C24 H28 N2 O6 S

L31 ANSWER 2 OF 4 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN

AN.S DCR-956381

DCSE 817201-2-0-0

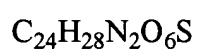
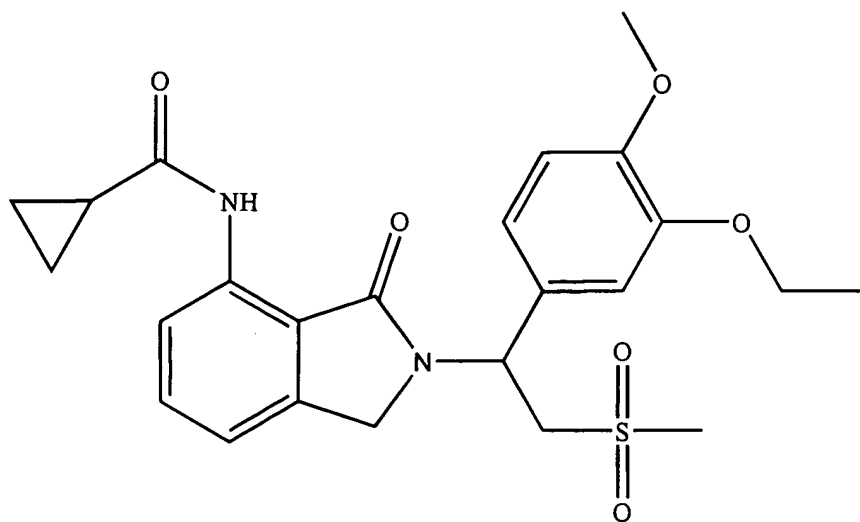
CN.S Cyclopropanecarboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide



MF C24 H28 N2 O6 S

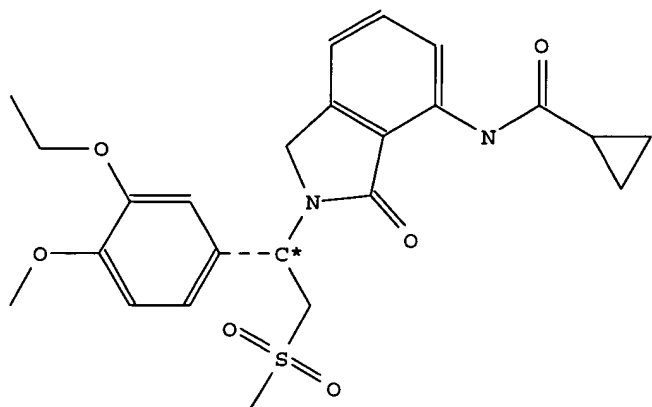
L31 ANSWER 3 OF 4 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN

AN.S DCR-956380



DCSE 817201-1-0-0

CN.S Cyclopropanecarboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide



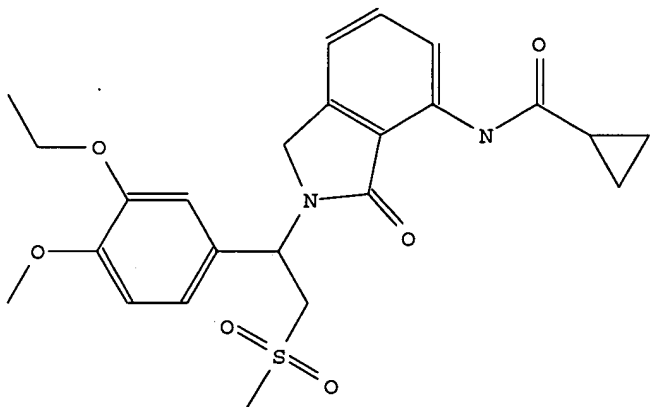
MF C24 H28 N2 O6 S

L31 ANSWER 4 OF 4 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN

AN.S DCR-817201

DCSE 817201-0-0-0

CN.S Cyclopropanecarboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl}-amide



MF C24 H28 N2 O6 S

=> d his

(FILE 'HOME' ENTERED AT 08:31:10 ON 20 JUL 2006)

FILE 'HCAPLUS' ENTERED AT 08:32:26 ON 20 JUL 2006

L1 1 US2006035955/PN OR (US2005-534325 OR WO2003-US35545)/AP, PRN
E ZELDIS J/AU

L2 93 E3-7
E CELGENE/CS, PA

L3 207 CELGENE/CS, PA

L4 18 CELGEN/CS, PA

noble jarrell 20/07/2006

FILE 'REGISTRY' ENTERED AT 08:34:19 ON 20 JUL 2006

FILE 'HCAPLUS' ENTERED AT 08:34:26 ON 20 JUL 2006
L5 TRA L1 1- RN : 21 TERMS

FILE 'REGISTRY' ENTERED AT 08:34:26 ON 20 JUL 2006
L6 21 SEA L5
L7 1 L6 AND C3/ES AND NC4-C6/ES AND 46.150.18/RID
L8 381 C24H28N2O6S
L9 3 L8 AND C3/ES AND NC4-C6/ES AND 46.150.18/RID
SAV TEM GEM325C3/A L9

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E ANGIOGENESIS/CT
L11 19056 E3-8
E E3+ALL
L12 19056 E7
E ANGIOGENESIS INHIBITORS/CT
E E3+ALL
L13 7571 E4
E E10
L14 2169 E3-6
E E3+ALL
L15 17954 E7+OLD,NT
L16 17 L10 AND L1-4
L17 5 L10,L16 AND L11-15

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L18 0 L9

FILE 'USPATFULL, USPAT2' ENTERED AT 08:45:01 ON 20 JUL 2006
L19 13 L9
E ANGIOGENESIS/CT
L20 5261 E3-4
L21 790 E5
L22 2 L19 AND L20-21

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FILE 'MEDLINE' ENTERED AT 08:46:13 ON 20 JUL 2006
L23 0 L9

FILE 'EMBASE' ENTERED AT 08:46:23 ON 20 JUL 2006
L24 0 L9

FILE 'BIOSIS' ENTERED AT 08:46:29 ON 20 JUL 2006
L25 0 L9

FILE 'WPIX' ENTERED AT 08:47:02 ON 20 JUL 2006
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EDIT /DCRE /DCSE
L27 21 E1-21
L28 1 DCR-817201/AN.S
L29 12 C24 H28 N2 O6 S/MF
L30 4 L29 AND (DCR-1178756 OR DCR-956381 OR DCR-956380 OR DCR-817201)
L31 4 L28,L30
SEL DCSE L31
EDIT /DCSE /DCRE
L32 10 E22-25
SEL SDCN L31
EDIT /SDCN /DCN
L33 10 E26-29
L34 10 L32-33

L35 . 10 L31/DCR
L36 10 L34-35
L37 3 L36 AND ?ANGIOGEN?
L38 3 L36 AND (B14-F02F? OR C14-F02F?)/MC
L39 5 L36 AND P52?/M0,M1,M2,M3,M4,M5,M6
L40 21259 A61P009/IPC, IC, ICM, ICS, ICA, ICI
L41 2 L36 AND L40
L42 5 L37-39, L41

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